Review Article

Medical Advice for Travelers

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Summary

Background: In 2019, 1.5 billion international tourist trips were counted worldwide. Germany, with 70.8 million vacations lasting ≥ 5 days, was one of the populations most willing to travel. These days, even elderly and multimorbid persons regularly travel long-distance, which can be associated with significant health risks. By advising travelers and implementing preventive measures, the risk of illness can be reduced significantly.

Methods: A selective survey of PubMed was performed to identify publications on medical advice for travelers between 2000 and 2020. We included guidelines, studies, and recommendations that mainly deal with the preventive aspects of travel medicine and have a high level of practical relevance and the highest possible level of evidence. Previously published guidelines (based on the GRADE criteria) were adopted, and recommendations not based on the results of scientific studies were characterized as Good Clinical Practice (GCP).

Results: Many medical recommendations for travelers still rely on individualized, experience-based, or consensus-based assessments. Apart from a review of medical history and vaccination status, a risk analysis is performed, travel fitness is evaluated individually, and a prevention plan is designed. Particular attention is devoted to malaria prophylaxis, vector protection, and traveler's diarrhea. Medical advice before travel is especially important for the elderly, children, pregnant women, the chronically ill, long-term and adventure travelers as well as migrants from malaria-endemic areas who are returning home.

Conclusion: The health risks associated with travel can be minimized by specialist medical advice. Many recommendations are empirical in nature and require further research.

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In 2019, 1.5 billion tourist trips were recorded worldwide (1). Germany, with 70.8 million tourist trips lasting longer than 5 days, was one of the nations most willing to travel. This willingness to travel is also increasingly seen among older and multimorbid individuals (1). Since there are no comprehensive systematic surveys on travel-related diseases in Germany, apart from the data provided by a handful of sentinel centers, it is difficult to draw valid conclusions about disease frequencies and entities (2). In a systematic literature review including nine studies from the USA and Europe, the proportion of travelers that acquired illness in the years 1985–2016 was 6–87% at an average trip duration of 8–21 days (3). Many of the relevant travel-related diseases, such as travelers' diarrhoea, skin disorders, as well as vector-borne and vaccine-preventable diseases, can be prevented or their risk reduced (4–6).

Method

A selective literature search was conducted in PubMed for publications in the period 2000–2020. The search included guidelines from scientific societies, as well as studies and recommendations primarily dealing with the preventive aspects of travel medicine (pretravel advice, vaccinations, fitness to travel, malaria prevention, vector protection, and prevention of travelers' diarrhea), while at the same time having high practical relevance and the highest possible level of evidence. Evidence was evaluated according to recommendations of the Agency for Healthcare Research and Quality (AHRQ). Previously published recommendations (based on GRADE [Grading of Recommendations, Assessment, Development and Evaluation] criteria) were adopted. Treatment methods that have been tried and tested in practice, as well as recommendations not based on the results of scientific studies, were characterized as Good Clinical Practice (GCP).

Procedure regarding medical advice for travelers

In routine practice, a structured and standardized approach has proven its worth (GCP) (7–9). Ideally, the consultation should take place 6, but at least 4, weeks prior to the travel start date, in order that certain travel vaccinations, for instance, can be completed. Even in the case of last-minute trips, important preventive measures such as health advice, malaria prevention, and vaccinations can still be carried out or initiated.

Cost clarification and consultation mandate

At the time of scheduling the appointment, or at the very latest before the consultation begins, the traveler

should be made aware of the fees that will be incurred (individual healthcare services)—even though many health insurance funds now cover the cost of travel vaccinations and malaria prophylaxis (10).

Travel analysis

In addition to destination and time period, important information includes: route(s), stopovers, reason, type and duration of the trip, means of transport used, (hotel) accommodation, previous travel experiences, and activities planned (for example, trekking, diving). Ideally, a detailed travel itinerary is provided.

Patient history and vaccination status

In order to carry out a risk analysis, a detailed medical history is required, including chronic, current, and travel-related illnesses (for example, fear of flying, kinetosis), previous surgical procedures, immune and vaccination status, medication, allergies, previous vaccination side effects and drug intolerances (for example, malaria prophylaxis), as well as pregnancy and health insurance status abroad.

Risk analysis and assessing fitness to travel

The assessment of fitness to travel is based on the risk of decompensation during travel (GCP). Important factors in this regard include medical care at the travel destination, risks of infection, standards of hygiene, climate, and potential preventive measures. Fitness for diving should be determined by a qualified diving physician (certified, for example, by the German Society for Diving and Hyperbaric Medicine [GTÜM]), taking into account the relevant recommendations (11).

To determine fitness to fly, it is important to assess the patient's overall clinical status. Exclusion criteria can be found in the airlines' conditions of carriage or in the International Air Transport Association (IATA) catalog (12). A British guideline and the US Centers for Disease Control and Prevention (CDC) also provide valuable information (13, 14). The following situations are examples of potential exclusion criteria:

- Highly contagious (untreated) infectious diseases
- Unstable angina pectoris
- Anemia (Hb level <8.5 g/dL)
- Within 3 days of acute myocardial infarction
- Pneumothorax
- Fresh or unsplit plaster cast
- Acute bleeding
- Acute psychoses within the preceding 30 days
- Pregnancy beyond 36 weeks (GCP).

According to a survey conducted in Germany of 2010 individuals aged over 14 years, 3% suffer from a fear of flying (aviophobia) (15). In the case of aviophobia, it can be helpful to actively address the subject of flying and fear (psychoeduction) and practice relaxation techniques in advance of travel (16). A seat on the aisle or near the aircraft wings should be preferred (GCP). In a randomized controlled trial with 69 participants, internet-based exposure treatment (*NO-FEAR Airlines*) was effective in all endpoints, such as the index score on the Fear of Flying Scale, compared to the control group (score difference: −17.23, $p < 0.001$; effect size: −1.51; 95% confidence interval [CI]: [−2.13; −0.71]) (17).

Children under the age of 5 years and pregnant women should not travel to malaria-endemic regions. An initial manifestation of malaria during pregnancy can pose significant risks to the mother and fetus (18). Young children can develop life-threatening organ complications such as cerebral malaria within hours of the first symptoms—or the disease manifests atypically (for example, without fever), thereby hampering the rapid initiation of treatment (19). Due to the risk of fetal malformations, pregnant women should also avoid traveling to areas with Zika virus outbreaks (20). Epilepsy patients should have long-term, stable seizure control and carry sufficient medication (GCP).

Individual prophylaxis plan

An individual prophylaxis plan includes the standard vaccinations recommended by the German Standing Commission on Vaccination (STIKO), as well as any travel-specific vaccinations indicated *(Table 1)* (21, 22). In the case of contraindications to yellow fever vaccination or other vaccinations, a medical exemption certificate can be issued.

For some destinations, it is essential to prescribe malaria chemoprophylaxis and recommend suitable repellents (23). In a small number of situations, for example, in the case of immunosuppression, chronic inflammatory bowel disease (IBD), or short trips involving high risk of infection, the prescription of prophylactic antibiotics can be considered (GCP). The carbonic anhydrase inhibitor acetazolamide is able to prevent acute mountain sickness (AMS) with a moderate level of evidence (relative risk [RR]: 0.47; [0.39; 0.56]; systematic review, 16 studies; 2301 participants) (24). When traveling to regions where there is high risk for travelers' diarrhea (for example, South and South-East Asia, Egypt), no first-aid kit should be without preparations for oral rehydration solutions (ORS) (25).

Deep vein thrombosis (DVT) prophylaxis using compression stockings and/or low-molecular-weight heparins or direct oral anticoagulants (DOACs; off-label use) is indicated in high-risk patients traveling on flights lasting more than 3 h—but is not generally recommended (26, 27). According to the randomized controlled trial (RCT) LONFLIT 5 JAP, the incidence rate of DVT with and without compression stockings was 0.97% versus 5.8%, respectively ($p<0.0025$; [28]). In the likewise randomized controlled LONFLIT3 study, the incidence rate of DVT with and without prophylactic heparinization was 0% versus 4.8%, respectively ($p < 0.05$; [29]). There are no RCTs to date on the use of DOACs in this indication (30).

For the prevention of seasickness and motion sickness, anticholinergics (for example, transdermal

TABLE 1

Overview of the most important travel vaccinations

Vaccination	Minimum age	Standard vaccination schedule or basic immunization (BI), route of administration	Immunity starting from
Hepatitis A	1–18 years, depending on the vaccine	1 × i.m.	> 2 weeks after BI
Hepatitis B	From birth	0–1–6 months i. m.	> 4 weeks after BI
Hepatitis A + B	1–16 years, depending on the vaccine	0–1–6 months i. m.	> 2 or 4 weeks after BI
TBE	1–16 years, depending on the vaccine	0–14 days to 9 months (after 2nd vaccine) i. m. 0–1–5 months (after 2nd vaccine) i. m.	2 weeks after 2nd vaccination for the current season
Meningococcal serogroups A, C, W_{135}, Y	6 weeks to 2 years, depending on the vaccine	1 × i.m.	> 1 week after BI
Meningococcal serogroup B	2 months or 10 years, depending on the vaccine	0–1 months i.m. or 0–6 months i. m.	Immediately after BI (2nd vaccination)
Rabies	From birth	0–7–21 (28) days i.m., rapid schedule *1: 0–3–7 days i. m.	2–4 weeks after BI
Polio	2 months	0–1–2 months i.m.	Immediately after BI (3rd dose)
Yellow fever	9 months	1 × s.c. preferred, see product information for i.m. injection	10 days after BI (consider for entry date)
Japanese encephalitis (JE)	2 months	0–28 days i.m., children < 3 years receive half-doses, rapid schedule*2: 0–7 days i. m.	4 weeks after BI
Typhoid fever	2 years (injectable vaccine)	1 × i.m.	14 days after BI
	5 years (oral vaccination)	0–2–4 days, orally; there should be a minimum interval of 3 days between the 3rd vaccination dose and start of malaria prophylaxis	> 10 days after BI
Typhus + hepatitis A	16 years	1 × i.m.	> 2 weeks after BI
Cholera	2–7 years, depending on the vaccine	1 x or 0–7(–14) days orally, maximum of 6-week interval between doses, otherwise new vaccination	7–10 days after BI, for at least 6 months

Overview of the vaccines most frequently used in Germany for travel medicine. The product information of the respective vaccines should be assessed prior to vaccination. A detailed and continuously updated summary, including rapid vaccination schedules and information on boosters, can be found in tabular form on the website of the authors' institution (www.uniklinikum-leipzig.de/einrichtungen/medizinische-klinik-2/infektions-und-tropenmedizin); for further details see (22).
*1 Only for adults aged 18–65 years (if the conventional pre-exposure prophylaxis schedule cannot be completed before the required vaccine protection within 21 or 28 days)
*2 Only for adults aged 18–65 years (if the conventional schedule cannot be completed before the required vaccine protection within 28 days)
i.m., intramuscular; s.c., subcutaneous

scopolamine) and antihistamines such as dimenhydrinate can be prescribed (31).

Education

The central aim of the consultation is to provide risk information based, as far as possible, on evidence, as well as to impart destination-specific health literacy skills. German nationals can only use the European Health Insurance Card, found on the back of the national health insurance card, to obtain medical services in travel destinations within the EU or in contracting countries (32). Good international health insurance should include pre-existing conditions, provide assistance services, and ensure "medically advisable and justifiable repatriation" (32).

In many countries, there are relevant health risks over and above infectious diseases, for example, as a result of road traffic, pollution, crime, and terrorism. The German Federal Foreign Office and other institutions provide information in this regard (list of information with useful internet addresses at www.uniklinikum-leipzig.de/einrichtungen/medizinische-klinik-2/infektions-und-tropenmedizin).

The consultation also includes instructions on hygiene and behavioral measures, as well as first aid in special situations, such as following animal bites, fever, diarrhea, or during stays at high altitudes. For example, rapid ascent to high altitudes (> 2500 m) can cause acute altitude sickness (AMS), the prevalence of which—depending on the study, age, absolute altitude reached, as well as the rate of ascent—can be as high as 30–45% even at moderate altitudes (3500 m) (33). If warning symptoms such as nausea, headache, or reduced performance fail to prompt a rapid descent, high-altitude cerebral edema (HACE) or high-altitude pulmonary edema (HAPE) may occur (34).

BOX 1

Warning symptoms and signs

- Unexplained fever (particularly following a stay in a malaria-endemic area)
- Diarrhea with bloody stools or fever
- Chronic (> 4 weeks) diarrhea
- Rash
- Petechiae
- Chronic (> 4 weeks), non-healing skin lesions
- Lymphadenopathy
- Hepato-/splenomegaly
- B-symptoms
- Unexplained blood count changes (for example, eosinophilia, thrombocytopenia, leukocytopenia)
- Unexplained elevation of liver values
- Unexplained (chronic) cough and persistent respiratory symptoms
- Myalgia, arthralgia
- Paresthesia, CNS symptoms
- Bleeding diathesis

Climate-related illnesses such as heat stroke, heat exhaustion/syncope, hypothermia, and frostbite can be prevented by means of a combination of acclimatization, appropriate behavior, suitable clothing, and sufficient intake of fluids, electrolytes, and food (GCP).

Time differences of more than 5 h result in disruption of the circadian rhythm in the form of jet lag (35). It has proven effective in practice to allow 1 day of adjustment time for every two time zones crossed on eastbound flights and 50% less when traveling westbound (GCP). In addition to sufficient sleep, it is considered beneficial to immediately participate in the local daily rhythm of the destination (involving time spent in daylight), avoid alcohol and sleeping pills, and refrain from strenuous activities during the first days of travel (12, 36). According to a systematic review with integrated meta-analysis, immediate-release melatonin (0.5–5 mg/day) is effective for the prevention and treatment of jet lag from a time difference of 5 h (RR jet lag score > 60: 0.5; [0.25; 0.74]; number needed to treat [NNT]: 2) (37, 38). As a physiological neurohormone, melatonin synchronizes the day–night rhythm via central and peripheral oscillators.

Finally, travelers should be familiar with the "ABC" of sun protection: avoidance, clothing, and sunscreen (39, 40).

Advice on follow-up care

The patient being consulted must be aware that travel-related illnesses can develop even after their trip. The most important warning signs and symptoms that should prompt (specialist) medical clarification are listed in *Box 1*. For example, any unexplained fever up to 4 months after returning from a malaria-endemic area requires clarification within 24 h.

Preventive measures

Medications and first-aid kit

Not all travel destinations allow travelers to bring medications into the country. If travelers are taking various active substances and medical items (for example, syringe needles) with them, it may be advisable to obtain a medical certificate (GCP). Ideally, this should be written in the languages of the countries to be visited/transited, but at least in English. Important medications and an informative medication list should always be carried in hand luggage; travelers should ensure that they take double the amount with them, distributed if possible over several pieces of luggage.

If the journey involves a time shift of more than three time zones, dosages of long-term medication(s), for example insulin and cortisone preparations, initially need to be adjusted (GCP): westbound air travel increases dose requirements due to the "longer day," whereas the "shorter day" with eastbound air travel reduces requirements (e1).

Box 2 provides an overview of the tried and tested first-aid kit.

Malaria prophylaxis

In Germany, approximately 1000 cases of imported malaria were registered annually between 2014 and 2019 (> 90% from sub-Saharan Africa) (e2). More than 70% of all imported cases involved the potentially life-threatening *Plasmodium falciparum* malaria. In 2019, of 814 cases with incomplete follow-up, only two deaths due to *Plasmodium falciparum* were registered (e2, e3).

The risk and severity of disease depend on numerous factors, including, among others, prevention compliance (23, e4–e8). According to a systematic review, the following adherence factors are beneficial for malaria prophylaxis:

- Higher age of travelers
- Shorter travel duration
- Good (previous) experiences with tolerability of anti-malarial drugs
- Going on a holiday rather than a business or adventure trip
- Seeking pretravel advice (e9).

Recommendations on prophylaxis should always be tailored to the individual (23). Consistent adherence to all preventive measures does not guarantee absolute safety—not even guideline-compliant malaria chemoprophylaxis is able to ensure this (for example, effectiveness of atovaquone/proguanil compared to placebo: 95.8%, [91.5; 97.9]; meta-analysis, 10 RCTs, 4539 participants) (e10).

BOX 2

Recommendations on additional basic items in a first-aid kit (indication/products)

- **Wounds, blisters, fractures/distortions**
  - Three gauze bandages 4/6/8 cm wide, respectively
  - One packet of sterile gauze
  - Cotton swabs
  - Band-aids 4 and 6 cm wide; two rolls (50 cm) of adhesive plaster in widths of 1.25 and 2.5 cm, respectively
  - Two elasticated bandage wraps 8 and 10 cm wide, respectively
  - 3–4 wound closure strips for cuts
  - Antiseptic wound gel or solution (e.g., povidone iodine, octenidine)
  - Tweezers
  - Tape, blister plasters, special padding material for plasters
  - A universal splint (foldable; in aluminum or plastic)
  - Triangular cloth
- **Hygiene, prevention, medical aids**
  - Mouth/nose protection masks
  - Hand disinfectant (e.g., in gel form), preferably alcohol-based
  - Condoms
  - 2–3 pairs of protective gloves
  - Scissors
  - Safety pin
  - Sufficient sunscreen agents (at least SPF 20; for children and fair-skinned people, at least SPF 30)
  - One emergency blanket (reflective)
  - Where applicable, ear drops for scuba divers for the prevention of otitis externa (containing ethanol, glycerol, glacial acetic acid)
- **Insect bites and stings**
  - Tick tweezers/fixing pin
  - Corticosteroid cream
  - Antihistamine cream (also available combined with hydrocortisone)
- **Pain and fever**
  - At least 10 tablets each of paracetamol/ibuprofen/novaminsulfone*1
  - Thermometer
  - For severe pain > 10 tramadol capsules (50 mg) or 10 tilidine tablets (50/4 mg)
- **Diarrhea**
  - Electrolyte mix for adults and children (in powder form to mix, and in fruit flavor for children)
  - Racecadotril, tannin albuminate/ethacridine lactate, loperamide (only as emergency medication)
  - Azithromycin, if necessary rifaximin/rifamycin (only after an appropriate risk–benefit assessment and in the case of non-invasive, non-bloody diarrhea without fever)
- **Abdominal pain (cramping)**
  - 5–10 butylscopolaminium bromide tablets
- **Nausea, vomiting, kinetosis**
  - 5–10 dimenhydrinate chewable tablets or 5–10 metoclopramide tablets, against kinetosis; alternatively, ginger tablets/chewing gum or scopolamine plaster
- **Cough**
  - 10 dihydrocodeine extended-release tablets or noscapine
- **Sunburn, skin and lip care/protection**
  - Bamipine lactate or flumetasone; dexpanthenol (skincare)—as gel, lotion, or spray
  - Sunscreen cream/pen (SPF 30–50)
- **Insect bite protection**
  - Repellents, preferably containing DEET or icaridin (as a precaution, purchased in home country); where appropriate, permethrin to treat clothing/mosquito net
- **Malaria protection**
  - Sufficient supply of tablets for malaria chemoprophylaxis or emergency treatment (purchased at a licensed pharmacy in home country to avoid counterfeits)
- **Individual own requirements/medication, doctor's letter**
  - Sufficient quantities of regular medications
  - Sun glasses and, where applicable, spare glasses
  - Where applicable, spare contact lenses and care products
  - Where applicable, monitoring devices (blood pressure, blood glucose, INR)*2
- **Acute mountain sickness (AMS) and high-altitude cerebral edema (HACE)**
  - 10 dexamethasone tablets 8 mg*3
- **High-altitude pulmonary edema (HAPE)**
  - 10 nifedipine extended-release tablets 20 mg*3
- **Angina**
  - 4–6 nitroglycerin capsules, nitroglycerin spray
- **Medical aids and devices**
  - Disposable syringes, 1–2 in each size: 2/5/10 mL, disposal hypodermic needles, 1–2 in different sizes (where applicable, with medical certificate)
  - Tourniquet
  - Rescue sheet (for evacuation of persons)
  - Stethoscope
  - Torch/penlight, alternatively, cellphone LED light

*1 No acetylsalicylic acid (ASS) due to risk of bleeding or complications (e.g., in the case of Dengue fever), ibuprofen also not recommended in suspected Dengue fever

*2 Where necessary, medical certificate and medication package inserts, doctor's letter in several languages, consider storage conditions (temperature range!) for medications and monitoring devices

*3 Information regarding indicated additional descent

AMS, acute mountain sickness, HACE, high-altitude cerebral edema; HAPE, high-altitude pulmonary edema; INR, international normalized ratio

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

The following measures can be recommended for antimalarial prophylaxis (14, 23, e11, e12):

- Exposure prophylaxis
- Long-term chemoprophylaxis
- Standby emergency treatment.

Insect bites should be consistently avoided around the clock (GCP). When traveling to high malaria risk areas, regular chemoprophylaxis is additionally indicated as a general rule *(Table 2, eTable, eFigure)* (23).

The criteria for standby emergency treatment (SBET) have been heavily restricted in the current guidelines, since travelers often encounter problems with its use. According to a meta-analysis by Tan et al., the overall pooled prevalence of indicated SBET among 26,403 travelers was only 2.5% ([1.1; 4.3%]; seven prospective cohort studies [e13]). If one assumes a malaria incidence of < 0.001% for low-incidence countries, the number needed to prescribe (NNP) is between 370 and 981 in order for SBET to be used in a judicious manner (e13). Added to this is the fact that many tourist regions are able to ensure the provision of ever better medical care (23). Therefore, SBET should only be prescribed for trips lasting longer than 7 days to areas with a low risk of malaria and poor medical care.

Vector control

To avoid insect and tick bites, as well as related diseases, the following measures of exposure prophylaxis are generally recommended (23, e14):

- Topical repellents *(Table 3)*
- Spatial repellents and insecticide sprays
- Light-colored, full-length, and closed clothing
- Bed nets—if necessary treated with insecticide
- Behavioral measures.

Repellents should not be applied until sunscreen products have had time to become effective (GCP). Particularly in malaria-endemic areas, it is beneficial to avoid outdoors at dusk and during the night as far as possible, and to instead stay indoors in mosquito-proof air-conditioned rooms, ideally protected by window and door grilles (e15, e16).

Prophylaxis and primary treatment of travelers' diarrhea

Acute travelers' diarrhea (TD) represents one of the most frequent health disorders experienced during long-distance travel, occurring in 10–40% of travelers in the first 2 weeks, depending on the destination, local microepidemiology, and style of travel (e17, e18). This applies in particular to South and Southeast Asia, as well as to West and Central Africa; backpackers tend to be more at risk than travelers staying in hotels (e19). The established rule of prevention "boil it, peel it, cook it, or forget it!" harbors problems of adherence and evidence. Nevertheless, travelers should be urged to observe good food and hand hygiene for plausibility reasons (GCP). Despite all "precautionary measures"

and even when staying in five-star hotels, it is not always possible to definitively prevent TD (e19). According to a systematic evidence review process in 2017 conducted by the International Society of Travel Medicine (ISTM), antibiotics should not be routinely used for TD prevention due to potential side effects and resistance induction (strong level of recommendation, low to very low level of evidence), although they could prevent an estimated 58–88% of all TD episodes (e20). Having said that, they can be considered for high-risk travelers (for example, those with inflammatory bowel disease [IBD] or immunosuppression) (strong recommendation, low to very low level of evidence) (e20). If indicated, rifaximin or bismuth subsalicylate (not available in Germany) are recommended for prophylaxis (strong recommendation, low to high level of evidence). According to a meta-analysis of four RCTs and 879 people, taking a daily dose of 400–600 mg of rifaximin can reduce the risk of disease by 47.8% ([37.5; 61.0], $p < 0.001$) (e21). Fluoroquinolones are not recommended by the ISTM for TD prevention due to potential side effects and high resistance selection pressure (strong recommendation, low to very low level of evidence) (e20). However, no antibiotic is currently approved for this indication. The evidence for prebiotics and probiotics in TD prevention is poor; only *Saccharomyces boulardii* has shown convincing effects to date (risk reduction: 79%, [72; 87], $p < 0.001$) (e22).

The effectiveness of live attenuated oral cholera vaccines through cross-protection in non-cholera-related TD is low (off-label use, maximum effectiveness: 7%; indeed, according to one Cochrane review, there was no significant effect at all) (e23, e24). Therefore, these vaccines should be reserved primarily for travelers staying in cholera outbreak areas or cholera-endemic regions with the most basic hygienic conditions (cholera prevention rate of approximately 85–90%) (e25, e26).

TD is predominantly bacterial in nature (72–80%, of which 28–42% are caused by enterotoxigenic *Escherichia coli*, ETEC) and is self-limiting within 48 h in over 50% of travelers, but nevertheless causes changes to travel plans and activities in 12–46% of those affected (e18, e19, e27). Severity is classified into:

- Mild (does not interfere with planned activities)
- Moderate (distressing and interferes with planned activities)
- Severe (heavily incapacitating, any form of bloody and/or febrile diarrhea) (e20).

Antibiotics should not be used in mild TD (strong recommendation, moderate level of evidence) (e20). Instead, loperamide or bismuth subsalicylate (not available in Germany) can be considered in adults (strong recommendation, moderate level of evidence) (e20). Antibiotic treatment may be performed for moderate TD (weak recommendation, moderate level of evidence), whereas it should be performed for severe TD (strong recommendation, high level of evidence) (e20). For empirical treatment, azithromycin is the preferred antibiotic, or rifaximin or rifamycin in the case of non-invasive pathogens. Fluoroquinolones can be considered with limitations (caution: high resistance rates in South/Southeast Asia) as a single dose or over 3 days (strong recommendation, high level of evidence) (e20).

This notwithstanding, a German consensus recommendation deems the enkephalinase inhibitor racecadotril to be the treatment of first choice—despite the lack of relevant studies on uncomplicated TD—since it does not affect the self-cleaning function of the intestine (in contrast to loperamide), can be used in all age groups, and has a lower interaction potential (e28). Activated charcoal (medicinal charcoal), although often found in first-aid kits, is not recommended by the ISTM or the German consensus paper due to a lack of efficacy studies.

TABLE 3

Important repellents/insecticides available in Germany

Active ingredient concentration	Repels mosquitoes for up to	Age restriction	Use during pregnancy
DEET (diethyltoluamide)			
30%	6 h	From 3 years*[1]	Insufficient data according to the manufacturer
50%	8 h	From 2 years*[1]	
Icaridin			
20%	6–12 h	From 6 months or 2 years depending on product*[1]	Possible depending on product (also while breastfeeding)
IR3535 (ethyl butylacetylaminopropionate, EBAAP)			
10%	4 h	From 2 months	Possible
20%	6 h	From 1 year	Possible
Oil of lemon eucalyptus (e.g., p-menthane-3,8-diol,, PMD)			
30%	6 h	From 1 year	Not specified
Permethrin (insecticide to treat textiles [clothing and bed nets])			
2%	4 weeks	From 3 years	Possible
5%	4 weeks	From 3 years	Not specified

Overview of important insect and tick repellents available in Germany.
Travelers should read the package leaflet before use. Not all repellents work equally well against mosquitoes, ticks, and bugs. The respective package leaflets provide information on this. The periods of duration of protection indicated for the individual repellents may vary according to environmental and personal factors. It is not uncommon for similar-sounding trade names to disguise different active ingredients. The table provides a non-evaluative selection of possible examples of products on the German market (modified from [23]).
*[1]DEET (30–50%) and icaridin are approved for use from as early as 2 months of age in many countries (e.g., Great Britain, USA).

Advice for risk groups

There are particular requirements on travel advice for the elderly, children, pregnant women, the chronically ill, long-term and adventure travelers (GCP), as well as migrants from malaria-endemic areas visiting friends and relatives (VFR). The latter group has a 2.82-fold increased risk of contracting malaria (95% CI [1.42; 5.92]) due to failure to take (sufficient) prophylaxis (e29).

According to §4 of the German Ordinance on Preventive Occupational Health Care (ArbMedVV) (e30), travelers are required to seek consultation with an occupational or tropical physician (German Social Accident Insurance [DGUV] principle G35) before or after occupational travel to countries with increased health risks. The employer bears the costs.

Conflict of interests
Dr. Wendt received reimbursement of congress fees and travel costs, as well as speaker's honoraria from the Centrum für Reisemedizin.
Prof. Lübbert received reimbursement of travel cost and speaker's honoraria from the Centrum für Reisemedizin.
The remaining authors declare that no conflict of interests exists.

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► **Supplementary material**

eReferences, eTable, eFigure:
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Supplementary material to:

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by Sebastian Wendt, Dietmar Beier, Dennis Paquet, Henning Trawinski, André Fuchs, and Christoph Lübbert

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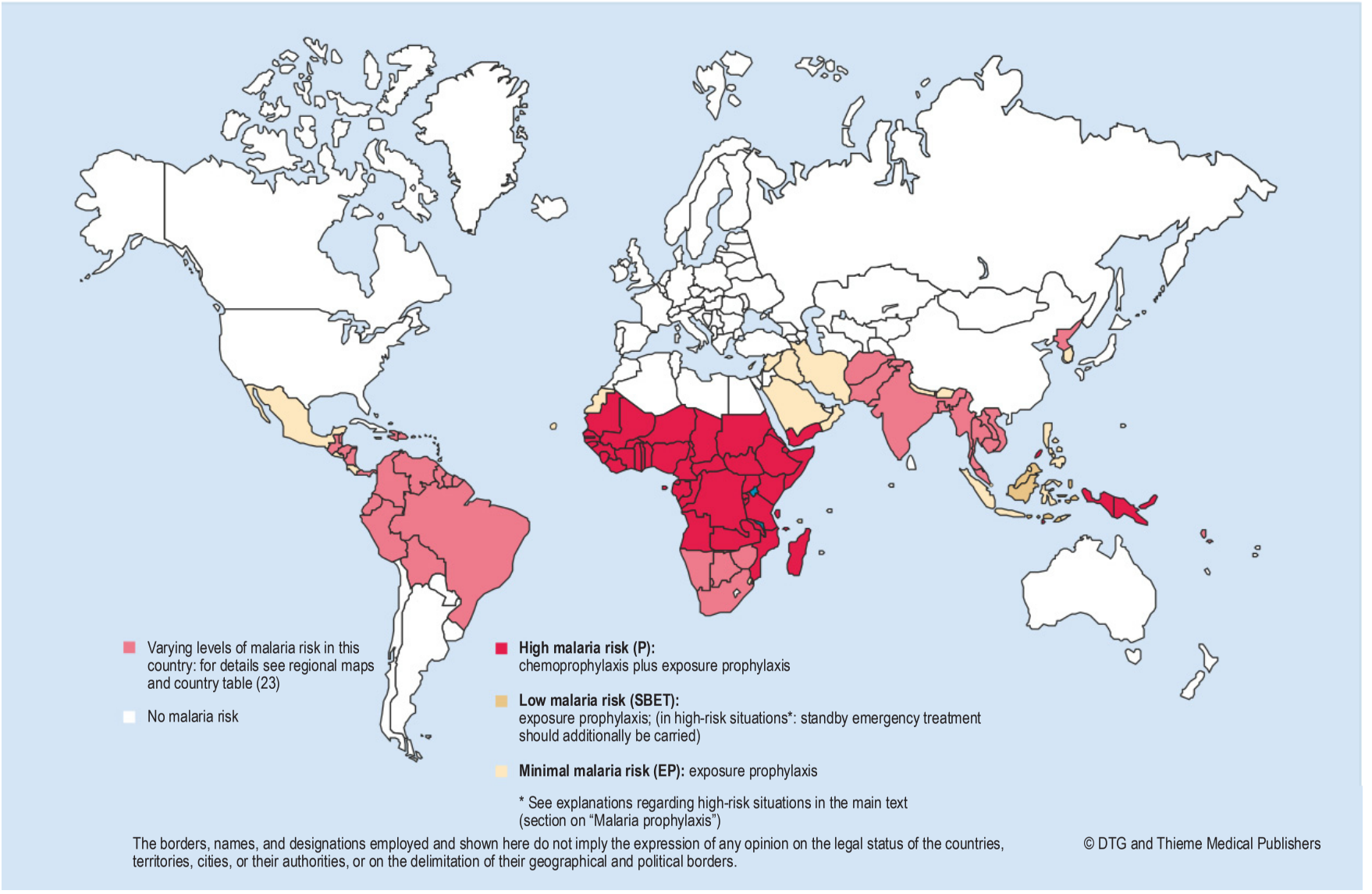
eTABLE

Weight-adjusted dosage recommendations on medications for malaria prophlaxis*[1] modified from (23)

Body weight (kg)	Age	Tablets/day Atovaquone/proguanil 62.5/25 mg (junior)*[2]	Tablets/day Doxycycline 100 mg*[2]	Tablets/week Mefloquine 250 mg*[2]
5–9	< 4 months	½ (up to 8 kg BW, off-label use)	–	⅛ tablet
9–11	4–11 months	¾ (from 8 kg BW, off-label use)	–	¼ tablet
11–15	1–2 years	1	–	¼ tablet
15–19	3–4 years	1	–	¼ + ⅛ tablet
19–25	5–7 years	1; or 2 from 21 kg BW	–	½ tablet
25–36	8–10 years	2; or 3 from 31 kg BW	½	½–¾ tablet
36–50	11–13 years	3 'junior' tablets; or 1 tablet for adults (250/100 mg) from 40 kg BW	¾	¾–1 tablet
> 50	> 13 years	1 tablet for adults (250/100 mg)	1	1 tablet

*[1] Atovaquone/proguanil (‚junior' formulation), doxycycline and mefloquine.
*[2] A commercially available pill splitter is recommended for pill splitting. Attention should always be paid to the respective valid product information.

eFIGURE



Recommendations on malaria prevention according to the German Society for Tropical Medicine, Travel Medicine and Global Health (DTG): overview map
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Questions on the article in issue 21/2021:

Medical Advice for Travelers

cme plus

The submission deadline is 27 May 2022. Only one answer is possible per question.
Please select the answer that is most appropriate.

Question 1

As a general rule, which individuals should be advised against traveling to malaria-endemic areas?

a) Pregnant women and women aged over 50 years
b) Men aged over 50 years and women aged under 20 years
c) Pregnant women and children aged under 5 years
d) Patients with chronic inflammatory bowel disease
e) Patients at risk of thrombosis

Question 2

What was the incidence of deep vein thrombosis in the LONFLIT3 randomized controlled trial with prophylactic heparinization versus no prophylaxis?

a) 0% versus 4.8%
b) 1% versus 5.8%
c) 3% versus 7.5%
d) 2% versus 10%
e) 5% versus 7.2%

Question 3

What is the time to onset of immunity following yellow fever vaccination?

a) Immediate
b) 5 Days
c) 10 Days
d) 3 Weeks
e) 4 Weeks

Question 4

How many cases of malaria were imported to Germany annually between 2014 and 2019?

a) Approximately 50
b) Approximately 200
c) Approximately 500
d) Approximately 1000
e) Approximately 2000

Question 5

In the case of oral vaccination against which disease is it important, when administering the third dose, to ensure that an interval of at least 3 days is allowed prior to the start of malaria prophylaxis?

a) Polio
b) Chickenpox
c) Yellow fever
d) Typhoid fever
e) Hepatitis A and B

Question 6

Acute altitude sickness can cause nausea, headaches, and reduced performance. Life-threatening complications are possible. In this context, what does the abbreviation HACE stand for?

a) High-altitude coronary embolism
a) High-altitude coronary embolism
c) High-altitude chronic encephalitis
d) High-altitude crisis and endocarditis
e) High-altitude cerebral edema

Question 7

Which of the following analgesics are not recommended in Dengue fever due to a risk of complications?

a) Tilidine
b) Acetylsalicylic acid
c) Pethidine
d) Novaminsulfon
e) Tramadol

Question 8

What advice should be given regarding repellents for insect bite prevention?

a) Repellents with DEET (purchased in Germany) should be used
b) Repellents should preferably be purchased at the travel destination
c) Use of repellents should preferably be avoided
d) Repellents should not contain icaridin
e) Plant-based repellents are preferred

Question 9

Travelers' diarrhea is a frequent problem during long-distance travel, particularly to South and Southeast Asia, as well as North, West, and Central Africa. When is the use of antibiotics recommended?

a) For prophylaxis as early as 2 days before the start of travel
b) For prophylaxis beginning on the day of arrival at the travel destination
c) For prophylaxis beginning 2 days after arrival at the travel destination
d) For the treatment of severe travelers' diarrhea
e) Antibiotics are contraindicated in travelers' diarrhea

Question 10

Which medication is recommended for both malaria prophylaxis and standby emergency treatment (SBET)?

a) Mefloquine
b) Artemether/lumefantrine
c) Doxycycline
d) Dihydroartemisinin–piperaquine
e) Atovaquone/proguanil