VILNIUS UNIVERSITY
MEDICAL FACULTY

The Final thesis

Vaccination of Travelers: Case Presentation, Vaccine-Preventable Travel Health Risks and Comparison of Vaccination Recommendations in Europe and the US

Keliautojų skiepijimas: atvejo pristatymas, vakcinomis kontroliuojama rizika keliautojų sveikatai ir skiepijimo rekomendacijų palyginimas Europoje ir JAV

Student Darwin Ghafar **Rahim, VI year, 3 group**

Department Clinic **of Infectious Diseases and Dermatovenerology**

Supervisor Prof. Dr. Ligita Jančorienė
(academic and scientific degree name surname)

Consultant (if applicable) _____

The Head of Department/Clinic Prof. Dr. Ligita Jančorienė

2024.05.10

Email of the student darwin.rahim@mf.stud.vu.lt

Table of Contents

1. ABSTRACT

This thesis examines vaccine-preventable diseases, focusing on travellers, emphasising the critical role of pre-travel consultations. Despite available preventive measures, vaccine-preventable diseases contribute to approximately 5.1 million deaths globally each year.

Through a review of the literature, this work explores the various dimensions of vaccine-preventable diseases, their epidemiological burden and effective prevention strategies that encompass both vaccination and non-vaccine measures. The practical application of this research is exemplified by a case study involving two elderly travellers embarking on a cruise across 30 countries. In preparation for their journey, both travellers were vaccinated against hepatitis A and B. Additionally, one traveller received a yellow fever vaccine, while the other was vaccinated against pneumococcal infection. Moreover, both travellers were advised on non-vaccine preventive measures and provided with malaria chemoprophylaxis and antibiotics to prevent traveller's diarrhoea. The thesis also examines variations in vaccination schedules between the different recommendations issued by the CDC, WHO, and ECDC on a national level. While different recommendations exhibit similarities in their immunisation schedules, they tailor these plans according to their specific epidemiological needs, resulting in noticeable differences. Considering these discrepancies, it is crucial for clinicians to carefully assess the travel risks and provide personalised recommendations for both vaccine and non-vaccine preventive measures. This tailored approach is essential to mitigate the impact of travel on global health and help reduce the significant toll of vaccine-preventable diseases, which continue to affect millions each year.

2. KEYWORDS

Vaccine-preventable Diseases, Pre-Travel Consultation, Vaccination Schedules, Immunisation of Travellers, Travel Medicine

3. INTRODUCTION

This thesis explores the role of vaccinations in guarding travellers against Vaccine-preventable diseases (VPD). Given that the epidemiological risks vary by destination, pre-travel consultations and adherence to vaccine schedules become more relevant to secure both personal and public health. This research aims to assess the value of being well-informed and prepared before travelling by reviewing the literature on vaccines, presenting a case, and taking a broader look at standard vaccine schedules. The goal is not to fearmonger but to encourage travellers to enjoy their global adventures safely and be equipped with the best preventive healthcare advice.

4. BACKGROUND INFORMATION

1. HISTORY

The history of vaccination has a remarkable impact on the story of medicine. It significantly influences socio-economic structures and illustrates a narrative of human suffering, innovation, inequality, collaboration, and hopes for a disease-reduced world.

The origins of vaccination are often conflated with inoculation, but modern medicine distinguishes between the two. Inoculation involves introducing a live pathogen to prevent disease, a practice predating vaccination rooted in the ancient strategy of variolation. It fostered the belief that surviving an illness grants lifelong immunity. However, the formal concept of vaccination began with Edward Jenner in the late 18th century. Jenner, often regarded as the father of vaccinology, observed that milkmaids who contracted the benign cowpox virus were immune to smallpox, a devastating disease of the time. In 1796, Jenner successfully demonstrated this theory by inoculating James Phipps, a milkmaid's son, with material from a cowpox lesion and later exposing him to smallpox; the boy did not contract the disease. This groundbreaking experiment, which would not meet today's ethical standards, marked the beginning of the smallpox vaccine and set the stage for modern immunisations.(1)

Figure 1: Dr. Edward Jenner performing vaccination -oil on canvas by Ernest Board

The next major advancement in vaccination came nearly a century later when Louis Pasteur developed the first laboratory-produced vaccine against Fowl Cholera in 1872.(2) This innovation led to several other vaccines, including yellow fever in 1937, pertussis in 1939, influenza in 1945, and polio in 1960. In 1967, the World Health Organization (WHO) intensified its efforts with the Smallpox Eradication Program, eradicating smallpox by 1980—a landmark achievement defined as the permanent reduction to zero of the global incidences of a disease.

Despite these successes, the battle against infectious diseases continues. By 2022, 14.3 million children worldwide had not received any vaccinations(3), and vaccine-preventable diseases (VPDs) still claim approximately 5.1 million lives annually.(4) The history of vaccinations reminds us of the powerful tools humans have created to face these challenges..

2. VACCINE CLASSIFICATION AND TYPES OF VACCINES

Attenuated Vaccines

In attenuated (live) vaccines, a weakened form of the pathogen is used, which, while able to replicate, cannot cause its original disease. As it mimics a natural infection, educating the immune system often takes just one shot. The efficacy springs from stimulating humoral and cellular defence mechanisms.(5) The drawback of this approach is the risk that the pathogen may become virulent in immunocompromised or pregnant patients. Examples of attenuated vaccines are yellow fever and typhoid, which are essential for people travelling to endemic areas.

Inactivated Vaccines

Inactivated vaccines contain pathogens that have been killed and cannot replicate, which is why a potential risk of infection is eliminated. The resulting immune reaction by the host is only humoral but not cellular. This allows for broad recommendations, even for pregnant and immunocompromised people. The main disadvantage of this mechanism is the short-lasting immunity resulting in multiple doses or boosters. Scientists use this necessity to adapt the vaccine to the current mutation of the virus, like a yearly influenza vaccine. Recommended inactivated vaccines in travel medicine are Hepatitis A, Polio, and Japanese Encephalitis.

Subunit, Recombinant, Polysaccharide, and Conjugate Vaccines

Subunit, recombinant, polysaccharide, and conjugate vaccines are a group of vaccine technologies that carry only a specific protein or sugar of a pathogen rather than the complete pathogen that the immune system makes best.

Subunit vaccines consist of purified protein subunits derived from the pathogen. They allow a targeted immune response without the risk of triggering disease. They are well tolerated but less effective because they do not carry other pathogen components.

Recombinant vaccines use genetic engineering techniques to produce antigenic proteins that resemble those on the pathogen's surface. This approach enables precise antigen selection and can elicit robust immune responses. However, their development process can be complex and time-consuming.

Polysaccharide vaccines contain polysaccharide molecules of the pathogen and stimulate an immune response by producing antibodies against these polysaccharide molecules. Although these vaccines are effective in some instances, they cause mild side effects in young children and immunocompromised individuals.

In conjugate vaccines, polysaccharide antigens are combined with carrier proteins to increase immunogenicity. Conjugate vaccines can stimulate both humoral and cellular immune responses by combining polysaccharides with proteins.

Toxoid Vaccines

Toxoid vaccines are vaccines aimed against bacteria that are producing toxins. During production, these harmful toxins are inactivated by heat or chemicals, and the now-called toxoids are ready for inoculation. The immune response will then be triggered not by the bacterium itself but by the harmless toxoids produced by a bacterium. These vaccines are safe to use but require boosters in 10-year intervals. While toxin-mediated diseases such as diphtheria, tetanus, and pertussis are not standard travel medicine vaccines, the ubiquity of these diseases and the number of travel-related injuries indicate checking the vaccination pass before travelling.

Viral Vector Vaccines

Viral Vector Vaccines are made of two components: a vector and the genetic information of the pathogen. The vector is a modified and harmless virus that has no virulence and causes no significant immune reaction. It functions solely as a "gene delivery system." The gene snippet in question belongs to the pathogen but only carries the protein's viral DNA on the pathogen's surface. Once inoculated, the vector invades the human cell and breaks down, facilitating a safe transport for genetic information. The host cell now produces this foreign protein and presents it to the immune system. This results in a strong humoral and cellular immune response without adjuvants needing to improve the response. If, however, the host already has built an immunity against the vector, the vaccine may lose its efficacy. The complex research and development behind it further limit this vaccine type. Diseases that a vaccine of this kind may prevent include COVID-19 and Ebola. The ladder one is of utmost importance for people travelling to endemic areas.

mRNA Vaccines

MRNA vaccines are similar to viral vector vaccines, which are made of two components. The vector, made of lipid nanoparticles, facilitates transportation. The encased genetic material, single-stranded mRNA, contains sequences to synthesise proteins, typically "spike" proteins on the virus surface. After inoculation, this vector fuses with the cell membrane, releasing the genetic information. The host's ribosome then produces the target proteins from the mRNA, leading to a potent immune response. However, long-term efficacy and safety data are still being gathered. Ultra-cold storage requirements present logistical and financial challenges, especially in remote and low-income areas, complicating future travel vaccination campaigns with mRNA vaccines. So far, only FDA-approved mRNA vaccines are against COVID-19, but their global success suggests they are promising for future vaccines.

It is essential to understand that every type of vaccine has its unique mechanism, benefits, and difficulties. Vaccines are vital in the overall public health scenario, especially in travel medicine, as they shield travellers from various diseases they may encounter.

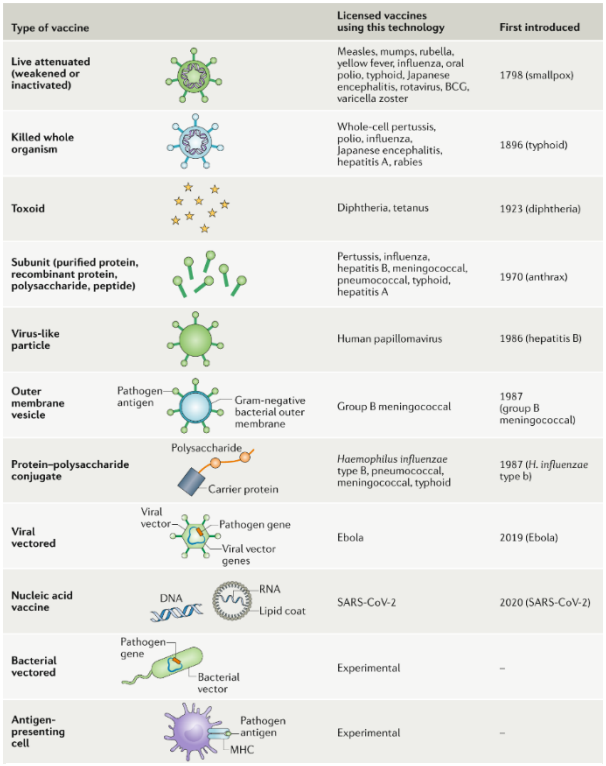


Figure 2: Different types of vaccine, Nature, A guide to vaccinology: from basic principles to new developments, 2020, ISSN 1474-1741

5. METHODOLOGY

1. RESEARCH SELECTION

The literature review aimed to collect and consolidate current and relevant research and guidelines on vaccine-preventable travel health risks and European and U.S. vaccination recommendations, specifically through the perspective of travellers. Primary sources included internationally recognised medical databases such as Tropimed and the CDC's Yellow Book, ensuring the information was authoritative and up to date.

Criteria for inclusion in the literature review were strict to maintain high academic standards. Only scholarly papers published in English or German from 2014 onwards were considered, ensuring relevance and contemporary perspectives in travel medicine. Similarly, guidelines on websites were only included if issued by national or international health authorities such as the WHO, the Centers for Disease Control and Prevention (CDC), the Robert Koch Institute (RKI), or the European Medicines Agency (EMA).

This methodology enabled an in-depth examination of current epidemiological challenges, vaccination strategies and their implementation in different regulatory environments, thereby providing an empirical basis for the case presentation.

2. CASE REPORT

The methodology for this case presentation involves the examination of a case involving two travellers, provided by the Department Clinic of Infectious Diseases and Dermatovenerology at Vilnius University Hospital Santaros Klinikos. The analysis focuses on applying both VPD vaccination and non-vaccine prevention strategies in the setting of a pre-travel consultation. Data was collected from clinical records and consultations, allowing a comprehensive review of the healthcare practices and adherence to international guidelines. Consent was secured from the individuals involved, allowing their case details to be published anonymously to protect their privacy and uphold ethical standards in research. The case presentation illustrates distinct challenges and considerations in vaccine recommendations for international travellers, connecting theoretical findings with practical outcomes by aligning them with current guidelines from WHO, CDC, RKI, and EMA, ultimately establishing best practice.

6. LITERATURE REVIEW

1. VACCINATION OF TRAVELERS

1. ROUTINE VACCINE CHECKUP

Routine immunisations are essential to travel preparation, especially for people visiting regions with endemic infectious diseases. Many vaccines are included in standard national immunisation programmes but should be checked for completeness of doses and adult boosters prior to travel. The pre-travel consultation provides a timely opportunity for healthcare providers to check the traveller's vaccination status. Booster shots are crucial to protect the health of both the individual and the community, especially considering the home country's immunisation schedule and the specific health risks associated with the destination. This proactive health measure is essential for safe and relaxed travel as it gives travellers and both communities peace of mind. In most cases, the primary immunisation in the vaccination schedule lasts a lifetime. Those that require a booster in adulthood are a combination immunisation of Diphtheria and tetanus (every ten years), influenza (annually), and tick-borne encephalitis (every three to five years). (6)

Diphtheria and tetanus

Diphtheria and tetanus are both severe bacterial infections that are preventable through vaccination. Diphtheria primarily affects the mucous membranes of the throat and nose, presenting symptoms such as a sore throat, fever, and a thick grey or white coating in the throat. Corynebacterium diphtheriae causes it and spreads via respiratory droplets. Tetanus, caused by Clostridium tetani, enters through wounds and produces toxins that lead to muscle stiffness and spasms, commonly starting with lockjaw. Treatment for both includes antitoxins and antibiotics, with tetanus treatment also involving muscle relaxants. The combined DTaP (Diphtheria, tetanus, and acellular pertussis) vaccine protects against both diseases in children, while adults require Td or Tdap boosters every ten years to maintain immunity. A complete series of the primary vaccine and the booster has a clinical efficacy of virtually 100% for tetanus and 97% for diphtheria. (7)

Influenza

Influenza, commonly known as the flu, is a contagious respiratory illness caused by influenza viruses A, B, and C; it typically presents with symptoms such as fever, cough, and sore throat. Treatment often involves antiviral medications and supportive care like rest and hydration. Transmission occurs through airborne particles from coughs or sneezes and contact with contaminated surfaces, peaking during winter in temperate climates and rainy seasons in tropical regions. Annually, influenza affects one billion people globally, making it the most infectious disease.(8) Vaccination, updated annually based on predicted virus strains, remains the most effective preventive measure, with efficacy rates ranging from 40% to 60%.(9) Vaccines recommended by the WHO for the 2023 season for the northern hemisphere included a quadrivalent inactivated vaccine for its minimal risk of side effects and effective annual adaptability.(10)

Table 1: Diseases, Routine Vaccination

Disease	**Transmission**	**Incubation**	**Mortality without Vaccination**	**Type of Vaccine**	**Vaccine Efficacy**	**Immunity Period**	**Non-Vaccine Prevention**
Diphtheria	Respiratory droplets	2–5 days	5%–10%	Toxoid Vaccine	High (Approx. 97%)	10 years (with boosters)	Antibiotics
Haemophilus influenzae type b	Respiratory droplets	Variable	High in children (if invasive)	Polysaccharide conjugate vaccine	High (95-100%)	Long-term	Avoidance of sick contacts
Hepatitis B	Blood, sexual contact, perinatal	60–150 days	15%–25% (chronic)	Recombinant vaccine	High (95%)	Long-term, possibly lifelong	Safe practices, screening
Human papillomavirus	Sexual contact, skin-to-skin	Months to years	Variable by cancer type	Recombinant vaccine	High (nearly 100% for some types)	Long-term	Safe sexual practices, screening
Influenza (seasonal)	Respiratory droplets	1–4 days	0.1%–0.2%	Inactivated & live attenuated vaccines	Moderate (40-60%)	Yearly (new strains annually)	Hand hygiene, antivirals
Measles, Mumps, Rubella	Respiratory droplets	Measles: 10–14 days	Measles: 0.1%	Live attenuated vaccine (MMR)	Very high (97-99%)	Lifetime with 2 doses	Isolation of cases
Pertussis	Respiratory droplets	7–10 days	0.5% in infants	Acellular vaccines (part of DTaP, Tdap)	High (80-90%)	5-10 years (with boosters)	Respiratory hygiene
Pneumococcal	Respiratory droplets	1–3 days	High in elderly & infants	Conjugate & polysaccharide vaccines	High (75-90%)	Varies by vaccine	Respiratory hygiene
Rotavirus	Fecal-oral	1–3 days	Low	Live attenuated oral vaccine	High (85-98%)	Several years	Hygiene, clean water
Tetanus	Contaminated wounds	3–21 days	10%–20%	Toxoid Vaccine	High (Approx. 95%)	10 years (with boosters)	Wound care, hygiene
Varicella (Chickenpox)	Respiratory droplets, contact	10–21 days	Low (higher in adults)	Live attenuated vaccine	High (94-98%)	Long-term	Isolation of cases

2. VACCINES RECOMMENDED FOR CERTAIN DESTINATIONS

These vaccines are recommended to protect travellers against diseases endemic to the destination country. They are intended to protect travellers and prevent disease spreading within and between countries.

Cholera

Cholera, caused by the Vibrio cholerae bacterium, occurs primarily in regions with poor water treatment, sanitation, and hygiene. The transmission of this enteric infection is primarily faecal-oral through consuming contaminated food or water. Symptoms develop within 1-5 days and include severe watery diarrhoea, vomiting and cramps, which can quickly lead to dehydration. Without immediate medical treatment, including rehydration and antibiotics, the mortality rate can exceed 70%, while prompt and adequate treatment reduces it to less than 1%. (11) Preventive measures are crucial in cholera-endemic areas. These include improving water quality and sanitation through WaSH (Water, Sanitation and Hygiene) initiatives and administering oral vaccines, which can achieve up to 90% effectiveness. (12) Despite the availability of prevention and treatment methods, cholera remains a significant global health threat, especially in economically weak regions. In 2019, cholera led to around 117,000 deaths worldwide, mainly in Africa. (13)

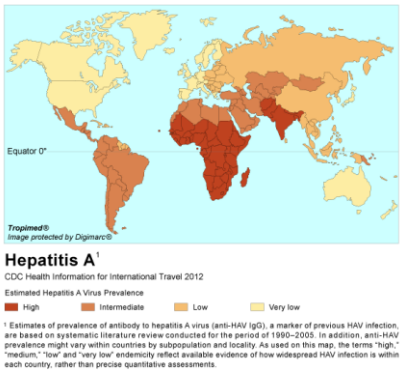


Figure 3: Hepatitis A Endemic Areas– World, Tropimed

Hepatitis A

Hepatitis A is, as its name suggests, an infection of the liver caused by a highly contagious virus named Hepatitis A Virus (HAV). HAV is transmittable through the fecal-oral route and primarily spreads via contaminated food and water in regions with inadequate sanitation. HAV is responsible for an estimated 1.4 million infections worldwide each year.(14) Symptoms range from mild fever and malaise to severe cases of jaundice, with a higher complication rate in adults over 50. While the overall mortality lies at 0.3%, it rises for > 40-year-old patients to 2,1%. (15) Vaccination is the most effective preventive measure against Hepatitis A. A two-dose series, beginning at twelve months of age and a booster dose six months later, is recommended. These vaccines are highly effective, offering over 94% protection.(16) Post-exposure prophylaxis within ten days of exposure is also crucial for unvaccinated individuals to prevent the disease. In addition to vaccination, travellers can prevent HAV by stringent hand hygiene and ensuring safe food and water consumption, particularly in high-risk areas.

Japanese encephalitis

Japanese encephalitis (JE) is a viral infection caused by the Japanese encephalitis virus (JEV). It is transmitted to humans through infected pigs via mosquito bites. (17) Most JE infections are asymptomatic, (18) however some patients experience flu-like symptoms in the initial phase, followed by a more severe phase affecting the central nervous system. Approximately 20-30% of patients with neurological symptoms succumb to the infection, and up to 50% of survivors suffer from permanent neurological damage.(19)

Currently, there is no specific antiviral therapy for JE, and treatment primarily consists of supportive measures. Preventive measures include using mosquito repellents, wearing long-sleeved clothing, and utilising mosquito nets. Vaccination is the most effective preventive measure, being over 96% effective(20) and is recommended for individuals living in or travelling to endemic areas.

Meningococcal disease

Meningococcal disease, primarily caused by Neisseria meningitidis serogroups A, B, C, W, and Y, spreads through respiratory droplets or close contact. Symptoms appear 3-4 days post-exposure(21) and include high fever, headache, rash, vomiting, and petechial exanthema. Untreated cases can lead to severe complications like brain damage and septic shock, with a general fatality rate of 1%, rising to 33% in cases of Waterhouse-Friderichsen Syndrome. The treatment involves antibiotics, but prevention through vaccination is crucial due to rapid progression. Recombinant vaccines targeting serotype B show efficacy of 95%-100%(22), while a quadrivalent vaccine is recommended for specific high-risk groups and travellers to endemic regions. The vaccine is mandatory for entry to Saudi Arabia and is further recommended for travellers to sub-Saharan Africa, especially the “Menigitis Belt” in Africa.

Polio

Polio, short for poliomyelitis, is a highly infectious viral disease caused by the poliovirus, affecting the motor neurons of the central nervous system (CNS). The virus spreads primarily through the fecal-oral route, particularly in areas with inadequate sanitation and hygiene practices. Incubation periods for polio typically range from 3 to 21 days, with 1% of infected becoming irreversibly paralysed, and up to 5% of those affected by paralytic polio die.(23)

Vaccination, particularly with Inactivated poliovirus and oral attenuated polio vaccine, boasting efficacy rates over 99%(23), remains pivotal in preventing polio transmission. In addition to vaccination, travellers are advised to practice good hygiene, such as regular handwashing and ensuring access to clean water and sanitation facilities, when travelling to endemic areas where polio transmission remains a threat.

Typhoid fever

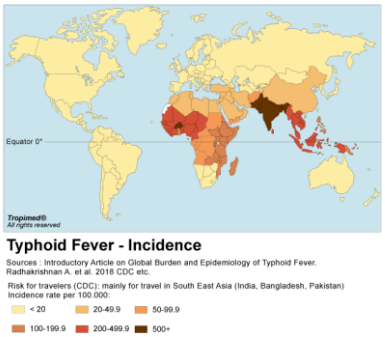


Figure 4: Typhoid Fever Endemic Areas – World, Tropimed

Typhoid fever is a bacterial infection caused by the bacterium *Salmonella enterica* serotype Typhi. As a fecal-orally transmittable disease, it spreads mainly through contaminated water and food. Symptoms, including fever, headaches, nausea, and abdominal pain, appear one to six weeks post-exposure. Diagnosis is through blood, bone marrow, or stool cultures, and treatment depends on antibiotics, considering antimicrobial resistance. Untreated, the disease can cause severe complications, highlighting the need for vaccination and better sanitation. Globally, typhoid affects about nine million people and causes 110,000 deaths annually, primarily in Western Africa and Southeast Asia. Rapid urbanisation and poor sanitation increase outbreak risks. Travellers to endemic areas should take preventive measures like vaccination and safe food and water practices. The WHO recommends primary vaccination with the Vi-TT conjugate vaccine for its 78.3% effectiveness.(24)

Rabies

Rabies is a deadly viral infection caused by the Rabies virus, a member of the Lyssavirus genus, with symptoms typically emerging three weeks to three months post-infection. Transmission occurs primarily through the bite or scratch of an infected animal, and once clinical symptoms appear, the disease is almost always fatal, with a mortality rate approaching 100%. Post-exposure prophylaxis (PEP) is required immediately, involving immediate wound washing, vaccination, and administration of rabies immunoglobulin or monoclonal antibodies. The WHO recommends three categories of contact with suspected rabid animals, each with specific PEP measures tailored to the level of exposure:

Table 2: Categories of contact and recommended post-exposure prophylaxis (PEP), Rabies, https://www.who.int/newsroom/fact-sheets/detail/rabies

Categories	Contact with suspect rabid animal	Post-exposure prophylaxis measures
Category I	touching or feeding animals, animal licks on intact skin (no exposure)	Washing of exposed skin surfaces, no PEP
Category II	nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure)	Wound washing and immediate vaccination
Category III	single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure)	Wound washing, immediate vaccination and administration of rabies immunoglobulin/monoclonal antibodies

"United Against Rabies" aims to eliminate dog-mediated human rabies deaths by 2030 by vaccinating dogs, which are the primary vectors in regions accounting for approximately 59,000 human deaths annually, primarily in Africa and Asia.(25) Until then, travellers, especially those venturing into regions where rabies is endemic, must avoid contact with unfamiliar animals and get vaccinated prior to the exposure if the contact is unavoidable.

TBE

Tick-borne encephalitis (TBE) is an arboviral infection caused by the tick-borne encephalitis virus (TBEV), primarily transmitted through bites of infected woodland ticks. Another less common mode of transmission is consuming unpasteurised milk from goats, sheep, and cows. While many TBE infections are asymptomatic, some patients develop biphasic symptoms, with the initial phase presenting flu-like symptoms one to two weeks post-exposure. Approximately 10% of adults and 5-30% of children progress to a severe phase affecting the central nervous system, resulting in meningitis or encephalitis, with a mortality rate of approximately 1% among patients with neurological symptoms. (26) Currently, no specific antiviral therapy exists for TBE, with treatment primarily involving supportive care. Vaccination is the most effective preventive measure, with efficacy rates between 96% and 98.7% after standard immunisation of three doses, with booster doses recommended at three years. (27) Travellers to endemic forested areas are advised to further reduce the chance of TBE by wearing protective clothing, doing daily tick checks for prompt removal, and avoiding unpasteurised dairy products.

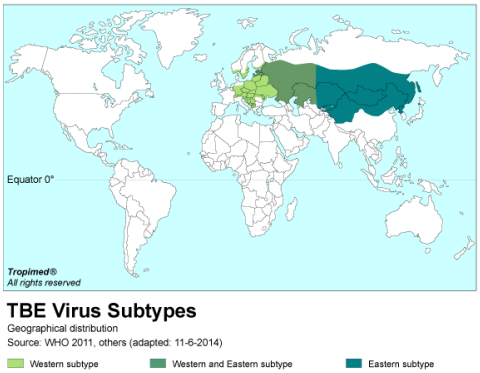


Figure 5: Tick-Borne Encephalitis Endemic Areas - World

Yellow fever

Yellow fever (YF) is a viral haemorrhagic disease primarily transmitted by infected Aedes or Haemagogus species mosquitoes, prevalent in tropical regions of Africa and South America. The incubation period ranges from 3 to 6 days, after which symptoms emerge, varying from mild fever to severe manifestations like haemorrhage and the name giving jaundice. Without vaccination, mortality rates from severe YF cases can reach up to 7%, highlighting the urgency of preventive measures.

Globally, YF accounts for an estimated 200,000 cases annually, resulting in approximately 30,000 deaths. To combat this threat, vaccination with the highly effective attenuated live vaccine "Stamaril" is recommended. This vaccine demonstrates exceptional efficacy, providing lifelong immunity in 99% of recipients. For travellers, particularly those visiting YF-endemic regions, vaccination is essential to prevent infection. Additionally, non-vaccine preventive strategies such as using insect repellent, wearing long-sleeved clothing, and staying in screened or air-conditioned accommodations can reduce the risk of mosquito bites.

Table 3: Diseases, Recommended Vaccination

Disease	**Transmission**	**Incubation**	**Mortality without Vaccination**	**Type of Vaccine**	**Vaccine Efficacy**	**Immunity Period**	**Non-Vaccine Prevention**
Cholera	Contaminated water and food	2 hours to 5 days	Up to 50% if untreated	Inactivated (oral)	80-90%	2 years	Safe water, sanitation
Hepatitis A	Contaminated food and water, close personal contact	Usually 14–28 days, up to 50 days	0.1% < 15 years 0.3% 15–39 years 2.1% ≥ 40 years	Inactivated	> 94%	Up to 20 years	Hand hygiene, safe food and water
Japanese Encephalitis	Mosquito-borne	5-15 days	20-30%	Live attenuated, Inactivated	> 96%	Lifetime with booster	Mosquito control
Meningococcal	Close contact, respiratory droplets	3-4 days	10-15%	Conjugate, polysaccharide, subunit	> 95%	3-5 years, booster recommended	Avoid close contact, hand hygiene
Polio	Fecal-oral, oral-oral	3-21 days	0,0005 %	Inactivated (IPV)	99 %	Lifetime with booster	Sanitation, hygiene
Rabies	Bites from infected animals	3 weeks to 3 months	Nearly 100% fatal	Inactivated	> 99%	Lifetime with pre/post-exposure	Avoid contact with stray dogs
Tick-borne Encephalitis	Tick bites	7-14 days	Up to 2%	Inactivated	> 90%	3 years with a booster	Tick avoidance, protective clothing
Typhoid fever	Contaminated food and water, fecal-oral	6-30 days	Up to 20%	Conjugate vaccine	78,3%	Oral vaccine: 5 years, Injectable vaccine: 2-3 years.	Hand hygiene, safe food and water
Yellow Fever	Mosquito-borne	3-6 days	4 – 7%	Live attenuated	99 %	Lifetime	Mosquito control

3. VACCINES REQUIRED FOR CERTAIN DESTINATIONS

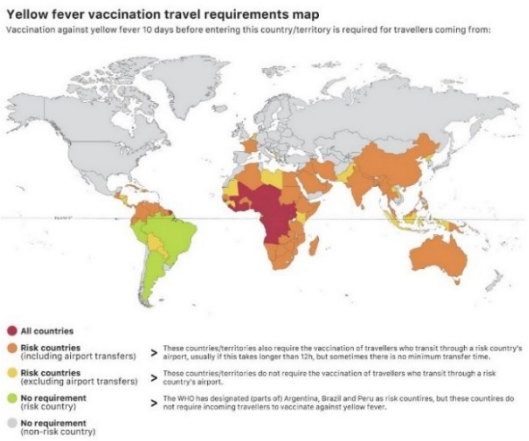


Figure 6: Vaccination requirements for international travel, Yellow Fever, 2019, WHO: International Travel and Health. Chapter 6 - Vaccine-preventable diseases and vaccines

Many countries have enforced compulsory vaccination mandates for travellers to contain the spread of diseases across borders. These requirements are determined by the prevalence of diseases in regions and their potential threat to public health. Presently, some countries mandate three vaccines for travellers. One such obligatory vaccine is the yellow fever (YF) vaccine for individuals visiting or returning from tropical South America and sub-Saharan Africa, where yellow fever is prevalent. In cases of fever without vaccination, the mortality rate can reach up to 20%. The Yellow fever vaccine offers immunity to 99% of recipients.

Similarly, the polio vaccination is compulsory for travellers entering or leaving countries identified as polio-endemic, polio-affected, or high-risk regions. Global efforts eradicated the Wild Polio Virus (WPV) almost entirely, with Afghanistan and Pakistan remaining the two countries still affected. (6 and 7 cases in the last 12 months)(28), underscoring the importance of vaccination for travellers to and from these areas. Moreover, several countries have polio vaccination guidelines for travellers to and from high-risk nations.

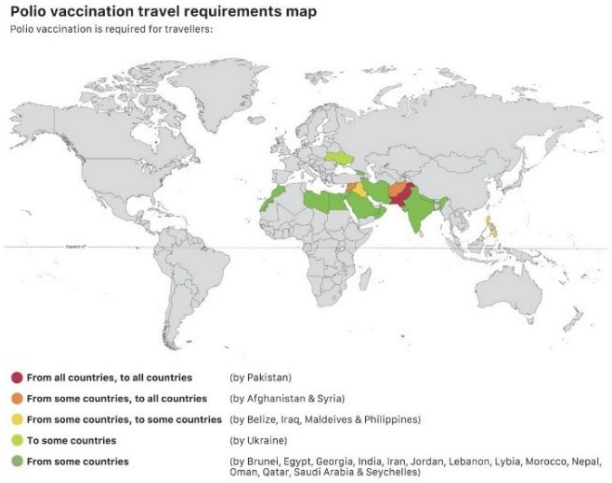


Figure 7: Vaccination requirements for international travel, Polio, 2019, WHO: International Travel and Health. Chapter 6 - Vaccine-preventable diseases and vaccines

Figure 8: Vaccination requirements for international travel, Meningococcal, 2019, WHO: International Travel and Health. Chapter 6 - Vaccine-preventable diseases and vaccines

The best-known example of a mandatory vaccine is the Saudi Arabian government's requirement that pilgrims attending the Hajj pilgrimage receive the Meningococcal disease vaccine. This requirement is based on the increased risk of disease transmission during gatherings at the Hajj, where close interactions among individuals can spread the illnesses rapidly. Meningococcal disease has a mortality rate of 10-15% if untreated, highlighting the role of vaccination as a preventive measure.

2. PRE-TRAVEL CONSULTATION

Before embarking on international travel, a pre-travel medical consultation is crucial, especially in regions like Africa and Asia, where up to 79% of travellers encounter health issues.(29) A consultation should be tailored to each traveller's health background, itinerary, trip duration, and planned activities, all determining their travel health risks. Healthcare professionals use this opportunity to educate travellers about potential hazards at their destinations and how to mitigate them, focusing on vaccination and non-vaccine prevention strategies and balancing health precautions with the positive aspects of travel.

3. TRAVEL RISK ASSESSMENT

1. ANAMNESIS

A pre-travel consultation relies on a thorough anamnesis. It should include a medical history, including detailed medical records, current medications, social background, travel experiences, and allergies, particularly to vaccine components like eggs. The goal is to determine if routine immunisations require boosters, and which specific travel vaccines are advisable. For individuals with existing medical conditions, assessing whether ongoing treatments like medication regimens, dialysis, or chemotherapy can be adequately maintained at the destination is essential. Special attention is needed for certain populations such as children, pregnant individuals, seniors, and the immunocompromised to tailor travel recommendations and preventive measures accordingly.

2. POPULAR ITINERARY

The itinerary is central for travellers' pre-travel consultation and preparation. Together with the patient, healthcare providers must analyse each region's health risks to tailor medical advice. This advice includes epidemiological data and considers political and environmental stability, healthcare infrastructure, and the impacts of climate change and seasonality on health risks. Pre-travel consultations should address common health issues and categorise risks based on environmental factors and disease prevalence. Given the diversity of environmental factors and illnesses and their prevalences, a categorisation needs to be done.

1. AFRICA AND THE MIDDLE EAST:

Due to their similar epidemiological and geographical profiles, the countries of Africa and the Middle East are grouped into one category. Before travelling to these areas, doctors should inform travellers about several diseases that can be prevented by vaccination or other protective measures.

The standard vaccination schedule and required boosters from the traveller's home country set the base for further vaccines. Additional vaccinations for cholera, chikungunya, dengue, Ebola, hepatitis A and B, rabies, polio, and typhoid are considered based on travel type and the regional epidemiological situation. Some countries require vaccinations like yellow fever and meningococcal vaccines, checked upon entry. Meningococcal immunisation is highly recommended in the "meningitis belt" to control epidemics.

In addition to vaccinations, other non-vaccine precautions are described further in 6.2.2: The main threats to travellers to this area are various mosquito species: Anopheles mosquitoes (malaria), Aedes mosquitoes (dengue fever, yellow fever, chikungunya, Zika virus), Culex

mosquitoes (West Nile fever). Using mosquito repellent, sleeping under insecticide-treated nets, and taking prophylactic anti-malarial medication prescribed by a doctor are crucial steps.

Figure 9: Malaria Endemic Countries – Africa, Tropimed

Food and water are another source of travel-related illnesses in the African-Arab region. Strict food and water safety precautions are necessary to avoid diseases such as cholera and typhoid. Travelers are advised to drink bottled or treated water, avoid ice cubes, and eat food that is thoroughly cooked and served hot.

In isolated regional areas in Africa and the Middle East, epidemic diseases such as Lassa fever, Rift Valley fever, and Middle East Respiratory Syndrome (MERS-CoV) are rare elsewhere. The increased risk of these diseases must be cautiously assessed in conjunction with the different healthcare infrastructure and potential political instability.

Irrespective of infectious diseases, travellers here must be careful due to extreme weather conditions, especially in desert regions. Heat-related Illnesses are easy to prevent if the recommendations are taken seriously.(30)

2. ASIA

With its diverse climate zones, densely populated cities, and different healthcare systems, the Asian continent poses a particular challenge for travellers. Various regions of this vast continent provide ideal conditions for various bacteria and viruses, posing an increased health risk for travellers, especially those visiting rural areas or staying for extended periods.

Polio is the only compulsory vaccination for entry into several North, East, and South Asian countries. As discussed in 6.1.3, WPT has yet to be eradicated in Afghanistan and Pakistan. Therefore, travellers to India from one of these countries must present their vaccination certificate.

Vaccinations against hepatitis A and B, diseases that are widespread in many Asian countries, are advisable. The poor hygienic conditions, especially regarding contaminated food, make it necessary for travellers to be vaccinated and avoid unwashed food and tap water. These preventive measures also help to reduce the risk of typhoid fever. Travellers need to be aware of rabies in rural areas of Asia, especially where medical care may be limited. Approximately half of the deaths from the disease (26000) occur in Asia, most of them in India. Prophylactic rabies vaccination is recommended for people who may encounter dogs and bats. Vaccination against Japanese encephalitis is recommended for travellers to rural areas of Southeast Asia and the Indian subcontinent during the monsoon season (May to October). In addition, you should use mosquito nets, insect repellent, and long-sleeved clothing to protect yourself from mosquito bites.

Figure 10: Japanese Encephalitis Endemic Areas – Asia, Tropimed

In addition to vaccinations, there are also non-vaccinal measures to protect against certain diseases. Avoiding mosquito bites is a high priority due to diseases such as dengue, chikungunya, and Japanese encephalitis. Using mosquito repellents, wearing long-sleeved clothing, and using mosquito nets are effective prevention strategies.(31)

Apart from infectious diseases, health issues may also be due to environmental factors. Depending on wind and regional air pollution conditions, travellers to urban areas in China or India may experience respiratory symptoms due to smog. In the continent's southeast, increased weather-related health risks such as natural disasters and heat-related illnesses in tropical areas are expected due to climate change. In contrast, in the east of the continent (China, Indonesia, Japan), travellers should be wary of earthquakes. Furthermore, travellers visiting popular high mountain regions in Asia should prepare for altitude sickness in the Himalayan regions.

3. THE AMERICAS AND THE CARIBBEAN

Figure 11: Malaria Endemic Countries – Americas, Tropimed

Travelers to the Americas and the Caribbean encounter unique health risks due to diverse climates and diseases. While vaccinations are not mandatory, yellow fever vaccination is strongly recommended due to significant risk, highlighted by Brazil's 2018 outbreak with 1,308 cases and 483 fatalities.(32) The Pan American Health Organization (PAHO) has included yellow fever vaccinations in the standard schedule from nine months of age.(33) Vaccinations for typhoid and hepatitis A are also advised because of the high rates linked to contaminated food and water. The region is home to the Anopheles mosquito, a malaria vector, with PAHO reporting 481,788 malaria cases and 92 deaths in 2022. Travelers must use mosquito bite prevention measures and drug-based prophylaxis.(34)

These systematic mosquito prevention measures also combat several arboviruses, including dengue, Zika, and chikungunya, necessitating the same meticulous use of mosquito repellents, wearing protective clothing, and accommodations in shielded environments. (35) Further measures regarding the dengue virus may include a vaccine approved only by the CDC in 2019. Although an attenuated vaccine named “Qdenga” for dengue is available, there is no general traveller recommendation; it is only explicitly recommended for individuals previously infected with the virus.

In November 2023, the chikungunya vaccine IxchiqTM received approval from the CDC and the EMA following two placebo-controlled trials, demonstrating that 98,9% of participants developed adequate antibodies.(36) The CDC’s Advisory Committee on Immunization Practices (ACIP) now endorses this vaccine for travellers visiting endemic areas, although the EMA has yet to issue a formal recommendation.(37) Travellers should consult healthcare providers for the most recent vaccination guidelines before departure.

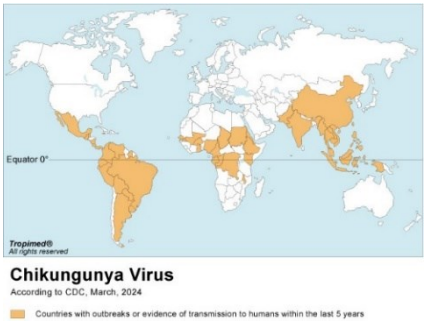


Figure 12: Chikungunya Fever Endemic Areas – World, Tropimed

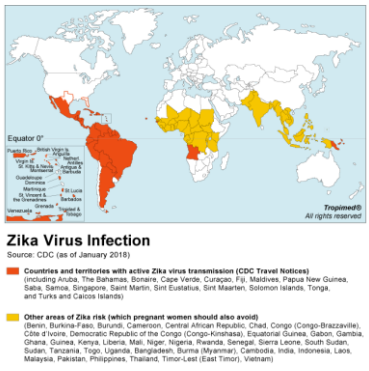


Figure 13: Zika Virus Infection Endemic Areas – World, Tropimed

There is currently no available vaccine for Zika. While most infections remain asymptomatic (80%), the virus poses a substantial risk to pregnant women as it can lead to conditions such as prenatal microcephaly or Guillain-Barré syndrome.(38) Moreover, exposure to water- and soil-borne diseases like leptospirosis and schistosomiasis remains a significant concern for those engaging in free water activities in contaminated settings. The most straightforward preventative measure against these infections is to avoid exposure to contaminated waters. For those at higher risk due to their activities, a prophylactic regimen of 200 mg of doxycycline weekly is advisable.(39)

3. ACTIVITIES

Evaluating and mitigating risky behaviours and communicating these risks with the patient is integral to a comprehensive pre-travel consultation. The medical assessments should cover various activities and potential risks to prepare travellers for upcoming challenges adequately.

Special attention is needed for mountaineering, diving, or hiking in remote areas. Assessing travellers' experience and fitness is vital. Beginners should use local guides to learn about safety equipment. Knowing the nearest medical facilities and emergency services also boosts travel safety.

Preparing for altitude sickness when travelling to high-altitude areas like mountains or ski resorts is vital. Travellers should acclimate slowly and recognise early symptoms like headaches, loss of appetite, and nausea. Critical conditions are acute mountain sickness (AMS) and high-altitude pulmonary oedema (HAPE) caused by rapid ascent. Prophylactic administration of acetazolamide (125 mg every 12 hours) is recommended, along with staying hydrated and avoiding alcohol. (40)

Wild animal encounters also present a significant health risk, mainly through the transmission of rabies. It is generally advised to avoid contact with unfamiliar animals. Nonetheless, if animal interaction is unavoidable in the itinerary, taking appropriate health precautions is crucial, especially for rabies. The viral disease is transmitted to humans primarily from bites from a rabid dog and is invariably fatal once clinical symptoms can be recognised.

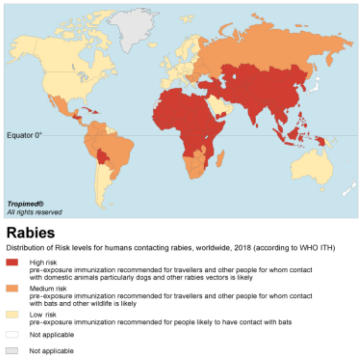


Figure 14: Rabies Endemic Areas – World, Tropimed

This includes avoiding contact with dogs, especially strays. However, if contact is unavoidable during the trip, live attenuated vaccinations will be administered as prophylaxis before travelling to endemic areas. Due to the high mortality rate, with 59,000 deaths reported annually in Africa and Asia, it is vital to inform the patient of the danger. (25)

The choice of accommodation also plays an essential role in the safety of travellers. Each accommodation type presents challenges and risks, from youth hostels and hotels to camping.

Shared facilities can compromise Personal safety and hygiene, so precautions such as avoiding shared bedding are necessary. Environmental factors and encounters with wild animals pose additional risks for those camping or staying in tents. It is essential to secure food supplies, use sturdy tents and be aware of local wildlife and weather conditions.

Travellers should be briefed on local safety protocols and conditions for water activities like swimming and boating. Using safety gear like life jackets and knowing about hazards like strong currents or venomous marine life reduces risks. As contaminated water may cause diseases like cholera and hepatitis A, bottled water for drinking and hygiene is recommended.

Culinary exploration while travelling presents its own set of risks. Adhering to straightforward guidelines by the CDC can significantly reduce the likelihood of foodborne illnesses. Tailored and meticulous pre-travel advice can enhance safety and overall well-being during international travel. Adequate preparation is key to preventing common travel-related health issues and injuries.

Table 4: Food precaution, 2024, CDC Yellow book 2024, Food and Water Precautions

High-risk foods	Strategies to avoid high-risk foods
Salads	Consume peeled fruits and vegetables.
Uncooked meat, fish, or eggs	Consume cooked food
Unpasteurised dairy products	Consume pasteurised dairy products.
Tap or well water, Products made using tap water or well water such as ice or juice	Consume water that is bottled and sealed or water that is disinfected (boiled, filtered, treated)
Food from street vendors	Be wary of food and water hygiene at eating establishment
Food served at room temperature.	Ensure meals are piping hot prior to consumption

4. NON-VACCINE PREVENTION

1. INSECT BITE

Pre-travel consultations are essential to address the significant health risks of insect bites during travel. Such bites can transmit diseases like Malaria, dengue, and Zika, which remain prevalent in tropical and subtropical regions. Epidemiologically, over 700 million people contract mosquito-borne diseases annually, resulting in more than a million deaths. (41) Therefore, educating travellers on effective repellent use, appropriate clothing, and behaviour modification during these consultations is crucial for reducing the risk of severe health issues abroad.

1. Insect Repellents: The Environment Protection Agency (EPA) of the USA has registered insect repellents with active ingredients such as DEET, picaridin, IR3535, or oil of lemon eucalyptus for protection against mosquitoes, ticks, and other biting insects. While studies have proven that repellents containing such ingredients are effective in repelling a variety of vectors responsible for transmitting diseases like Malaria, dengue, Zika, and chikungunya, the problem lies not in the repellent but in the inadequate application. One study has shown that only 2,5% of travellers applied the recommended protective dose of repellent.(42) To ensure proper anti-vectorial protective measures (AVPM), patients should be educated on the repellent's specific quantitative and qualitative use and the possible side effects, such as a

burning sensation on the skin and reddening of the skin. These latter often lead to improper usage, particularly in young and inexperienced travellers. Ideal application rules(43):

- Apply just enough repellent to cover exposed skin.
- Avoid over-applying repellents.
- Follow label directions to find out how long to wait before reapplying.
- Do not use under clothing.
- Do not apply on open cuts or irritated or sunburned skin.
- Do not spray repellents on the face, in the ears, or near the eyes or mouth. To apply repellent to the face, apply it to the hands and then rub it onto the face.
- Wash skin and treated clothing when returning indoors.
- Wash clothing prior to wearing it again.
- Mixing a repellent with sunscreen can affect how the skin absorbs the products. (44)

2. Protective Clothing: Light-coloured, long-sleeved shirts and pants treated with permethrin can shield against mosquito bites, ticks, and stings from bees and wasps. Permethrin treatment remains effective through several washes and can also repel and kill Aedes aegypti, the vector of yellow fever diseases (45) and prevent Malaria by up to 50% (46).

3. Environmental Controls: Ensure that accommodation is secured with air conditioning and intact screens on windows and doors to keep mosquitoes out. Using long-lasting insecticidal nets, especially in areas prone to Malaria or other mosquito-borne diseases, has been proven to reduce the incidence of Malaria by up to 56%. (47)

4. Behavioural Adjustments: Avoid outdoor activities during peak biting times for mosquitoes (dusk to dawn) and in areas where scorpions or snakes may be present. Do not walk barefoot or reach under rocks and logs where scorpions may hide. Avoid wearing bright colours or floral scents to prevent bee and wasp stings. Those with severe allergies should carry epinephrine auto-injectors. For scorpion stings, immediate medical attention is necessary, particularly in areas with dangerous species. Scorpions often hide in shoes and clothing, so shaking out these items before wearing them is advisable. These precautions can help manage and reduce the risks associated with stings and bites. (48)

6. Snake Bites: Travelers to sub-Saharan Africa, South Asia, and Southeast Asia face higher risks of snake bites.(49) Protective measures are crucial, such as wearing boots and long trousers and using flashlights at night. Awareness of local snake species, their behaviours and common location can enhance safety. In the event of a snake bite, immobilising the affected limb and promptly seeking medical help is essential; immediate treatment is critical, as traditional first aid methods are ineffective. Detailed prevention strategies and understanding regional epidemiology are vital for reducing snake bite incidents during travel.

2. FOOD AND WATER

Pre-travel consultations are crucial in safeguarding travellers against food and water-related illnesses, which remain a global health concern. The pre-travel consultations should provide essential guidelines on minimising the risk of acquiring such illnesses through proper food and water safety measures.

Traveller's diarrhoea

The estimation of how many travellers suffer from traveller's diarrhoea (TD) varies from 30% to 70%, depending on the itinerary, but it is prevalent virtually everywhere on Earth. TD is predominantly caused by pathogenic bacteria such as Escherichia coli (particularly Enterotoxigenic E. coli or ETEC), with Campylobacter jejuni, Shigella spp., and Salmonella spp. also contributing significantly. (50)

TD is categorised by the severity and the duration of symptoms. While most cases are mild and can be managed with rehydration, mainly using Oral Rehydration Salts (ORS), more severe cases require antibiotics such as azithromycin or fluoroquinolones.

Table 5: Treatment of Travelers' Diarrhoea, Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report, 2017,

Severity	Symptoms	Treatment Recommendations
Mild	Tolerable, not distressing, does not disrupt activities	Loperamide or BSS may be considered
Moderate	Distressing, interferes with activities	Antibiotics like Azithromycin or Rifaximin; Loperamide as adjunctive therapy
Severe	Incapacitating prevents activities, including dysentery	Azithromycin preferred; Fluoroquinolones or Rifaximin for no dysenteric cases
Persistent	Lasting ≥2 weeks	Microbiologic testing is recommended; follow-up is necessary

To prevent TD, travellers are advised to adhere to stringent food and water safety practices. This includes consuming only food cooked and served hot, avoiding raw or undercooked meats and seafood, and avoiding unrefrigerated dairy products. Drinking only bottled, boiled, or chemically treated water is crucial, as is avoiding ice cubes from questionable sources.

Water quality

When travelling to areas with questionable water quality, it is essential to use various methods to ensure water safety and prevent waterborne diseases. These diseases can be caused by bacteria such as E. coli, Salmonella, and Vibrio cholerae, viruses such as Hepatitis A, and parasites such as Giardia and Cryptosporidium.

Due to its superior purification, factory-sealed bottled water is the ideal water source. If unavailable, travellers have several household water treatment (HWT) options. Boiling is the most reliable, requiring one minute at lower altitudes and three minutes above 2,000 meters to kill pathogens.(51) Chemical disinfection with iodine is effective but less so against parasites like Cryptosporidium. Users of iodine tablets and tinctures must adjust the dosage based on water temperature and clarity and be aware of health risks such as thyroid issues, particularly for those with unstable thyroid function, iodine allergies, or pregnant women.(52) Filter systems, including microfilters and reverse osmosis, are another purification method. They target organisms like viruses and parasites, including Giardia and Cryptosporidium.

By using these purification techniques, travellers can significantly reduce their risk of waterborne diseases and have a safer, more enjoyable travel experience.

7. CASE PRESENTATIONS

1. TRAVEL RISK ASSESSMENT

The following chapter discusses the case of 2 patients consulted by an infectologist in November of 2023 because of a cruise ship trip visiting 30 countries within four months.

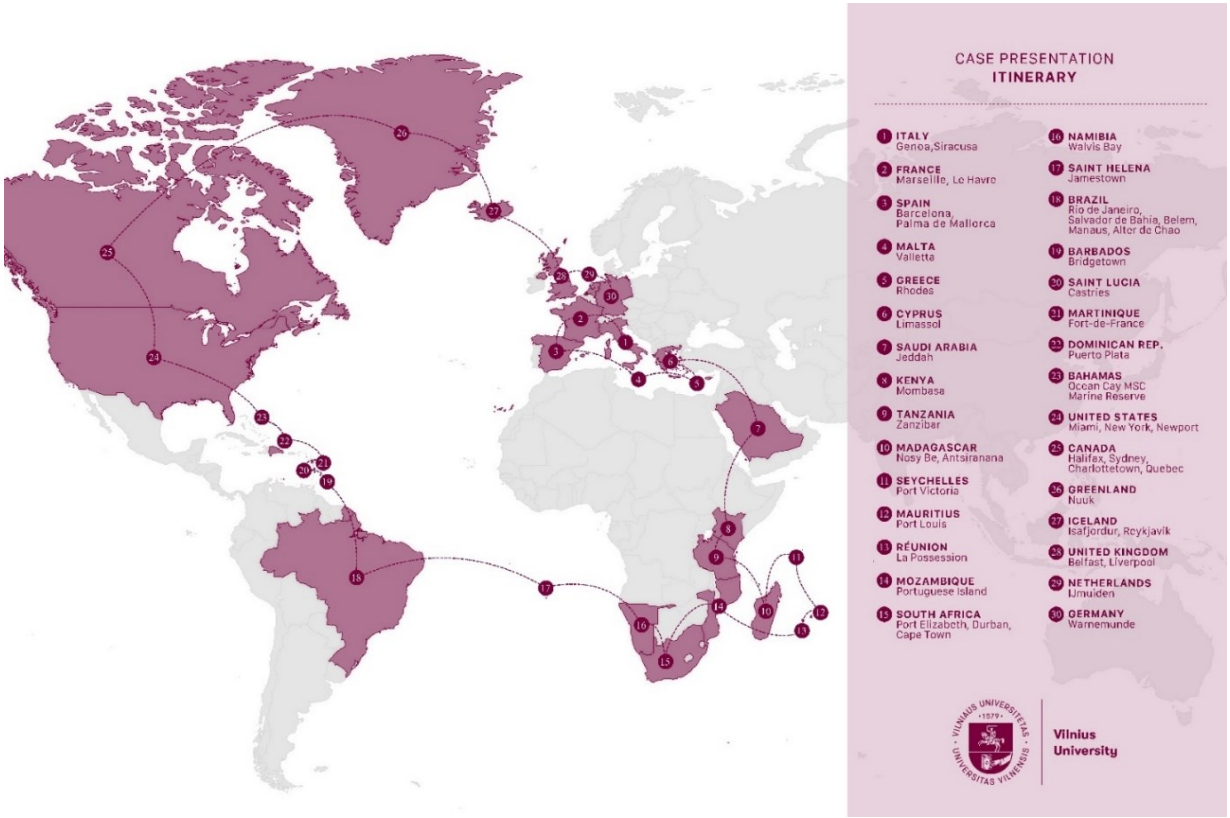
1. ANAMNESIS

Traveller 1: Female, born in April 1948. She presents in a fit, age-appropriate condition with no acute complaints, significant disease history, or known allergies. She is fully vaccinated according to the Lithuanian schedule and was vaccinated in 2018 with the Dultavax vaccine against diphtheria, tetanus and polio and received two doses of Twinrix against Hepatitis A and B.

Traveller 2: Male, born in August 1944. He also presents in a fit, age-appropriate condition with no acute complaints, significant disease history, or known allergies. He is equally fully vaccinated according to the standard Lithuanian schedule and received the same vaccinations in 2018. He has additionally been in 2008 against Yellow Fever.

2. ITINERARY

The couple has mapped out an itinerary involving visiting 30 countries and two popular itinerary regions already covered in 7.1.1.2: Africa and the Middle East, as well as the Americas and the Caribbean. On this remarkable global tour, they will experience diverse climates, cultures, and epidemiological environments, exposing them to different health risks.



3. ACTIVITIES

The trip of the 75- and 79-year-old travellers will be based around the activities off and on the cruise boat, where they have their airconditioned bedroom. It is doubtful that they will engage in adventurous physical activity that may put them in danger. While a safari may be planned in Africa, only a locally guided touristic safari will be an option. Swimming in the ocean or lakes is planned, but only when local authorities authorise it. While food is served on the boat, the travellers are looking forward to trying the local cuisine, guided by a tour guide.

2. INDIVIDUAL VACCINATION PLAN

Table 6: Vaccination Plan for Case Travellers

Vaccine against	**Vaccination indication**	**Recommended for case travellers**
Cholera	For travellers to areas of active cholera transmission, with inadequate water treatment and hygiene.	No
Hepatitis A	For travellers visiting endemic countries, especially in rural areas, consuming potentially unhygienic foods and water	Yes
Japanese Encephalitis	For travellers to endemic areas in Asia and the Western Pacific • for a prolonged time (>1 month) • working near rice fields and pig farms	No
Meningococcal	For travellers: • visiting areas in the meningitis belt during the dry season (December to June). • visiting Mecca during the Hajj (quadrivalent vaccine required)	No
Polio	For travellers: • to endemic countries with WPV or vaccine-derived poliovirus (VDPV) is actively circulating • engaging in humanitarian work at refugee camps in areas adjacent to endemic areas	Yes
Rabies	For travellers to endemic countries: • with contact with wild dogs or bats • staying remotely or engaging extensively in outdoor activities in rural areas	No
Tick-borne Encephalitis	For travellers to endemic countries with exposure to ticks in warm weather months April-November)	No
Typhoid fever	For travellers to endemic areas with prolonged stays	No
Yellow Fever	For all travellers visiting endemic zones. Some countries also require it for entry into certain countries.	Yes

Based on a comprehensive review of the literature, patient history, and travel itinerary, it is suggested that Patient 1 should get their third dose of the Twinrix vaccine along with the Stamaril vaccine. Twinrix is a dual vaccine, carrying hepatitis A (inactivated) and hepatitis B (recombinant) components to protect from both infections. Stamaril, on the other hand, is used to prevent yellow fever and is a live attenuated viral vaccine despite the different vaccination technologies. Both vaccines can be administered simultaneously, although at different injection sites, without interference in immune response or increased adverse reactions.

Patient 2, considering the same travel destination factors, is also recommended to be administered the third dose of Twinrix for added protection against Hepatitis A and B. Stamaril; however, it is not needed, as the patient has been previously vaccinated for yellow fever. Next to the Twinrix, Patient 2 should also receive a booster shot of the Prevenar 13 vaccine. This polysaccharide conjugate vaccine guards against infections caused by the pneumococcal virus. For example, in patient 1's case, these vaccines can be given simultaneously, with different injection sites, without any worries about interference with immunity. Even though the side effects of these vaccines are generally mild, it's advisable to keep an eye on the injection sites for any signs of inflammation or unusual responses. It's crucial to ensure every patient gets the correct vaccination records for yellow fever, as some countries may require this documentation for entry.

3. NON-VACCINE PREVENTION

In alignment with the general non-vaccine prevention recommendations outlined in section 6.2 of this thesis, it is essential to adapt these strategies to each patient. Given the anamnesis, itinerary, and activities, the patients should predominantly be consulted regarding preventing insect bites, heat-related illness, and environmental exposure. For malaria, the couple should receive chemoprophylaxis with Malarone (atovaquone/proguanil), taking one tablet daily, starting the day before arriving in Saudi Arabia and continuing until the seventh day after leaving the Dominican Republic. Regarding food and water safety, they must be cautious to avoid traveller's diarrhoea and other foodborne illnesses. They should consume only bottled or purified water and eat well-cooked meals. (*Table 4*) Should travellers' diarrhoea occur, they are advised to take Azithromycin 500 mg once daily for three days to manage the symptoms and minimise discomfort during their trip. These individualised measures are effective in ensuring a safe and healthy travel experience.

8. STANDARD VACCINATION SCHEDULES

1. EUROPEAN AND US GUIDELINES

The standard vaccination schedules of the United States and Lithuania exhibit similarities and notable differences, reflecting each country's public health strategies and disease prevalence. Both nations prioritise essential early childhood vaccinations such as Hepatitis B, DTaP/Tdap, Hib, PCV, MMR, Rotavirus and HPV in later childhood, spotlighting a shared recognition of these vaccines' impact on public health. However, certain vaccines' schedules do not match tuberculosis (TB), varicella, hepatitis A, and influenza. When analysed narrowly, it becomes clear how epidemiological trends and healthcare priorities influence public health policies.

In Lithuania, the BCG vaccine is given to newborns as a measure to combat TB, reflecting the higher rates of tuberculosis in comparison to the United States. In 2019, Lithuania had a higher incidence of TB than the U.S., with about 29 cases per 100,000 people (53) versus around 2.5 cases per 100,000 people in the U.S.(54) This significant difference explains why Lithuania continues using the BCG vaccine since it aligns with WHO recommendations for countries facing a burden of TB.

The following discrepancy concerns varicella (chickenpox). The U.S. advocates for two-dose varicella vaccination to prevent initial outbreaks and reduce severity, and this strategy has been successful. (55) On the other hand, Lithuania does not currently include varicella vaccination in its standard national immunisation plan. One reason could be the lower incidence rate, with 14504 reported cases in 2022.(56) Another reason may be the cost-effectiveness evaluations when considering this vaccine's widespread implementation, as one study values Lithuania's total economic burden of varicella at 1,620,000€. (57)

Two further vaccines often associated with travellers are hepatitis A and influenza vaccines. In the U.S., children aged 12-23 months routinely receive hepatitis A vaccination due to past outbreaks and potential risks for travellers. Possibly because of lower incidence rates or different public health assessments, the vaccine is not routinely given in Lithuania.

The last difference is in the recommendation of influenza vaccines. While the U.S. recommends vaccination for all individuals over six months old, Lithuania focuses its influenza vaccination efforts on high-risk groups like healthcare workers, the elderly, and the immunocompromised, as they are deemed more vulnerable to severe illness from influenza.

This comparison does not intend to deem an objectively superior schedule but to highlight how countries tailor their public health approaches based on health benefits, health risks, and disease prevalence.

Table 7: Comparison of Standard Vaccination Schedules of the U.S and Lithuania, US schedule by CDC, Lithuania schedule by ECDC

Vaccine	United States	Lithuania
BCG (TB)		X
Hepatitis B	X	X
DTaP/Tdap	X	X
Hib	X	X
PCV	X	X
MMR	X	X
Rotavirus	X	X
Varicella	X	
Hepatitis A	X	
Meningococcal	X	
HPV	X	X

9. DISCUSSION

The literature review covered aspects ranging from vaccination efficacy to various preventative measures. The findings from the case study highlight the importance of pre-travel consultations in addressing individual health needs, in this case, those of elderly travellers, a demographic shown to be at increased risk for travel-related illnesses.(58) The consultations for the travellers, scheduled two months before departure, were instrumental in updating essential vaccinations such as Hepatitis A and yellow fever, preventing severe diseases during travel. These interventions align with best practices in travel medicine, emphasising vaccination, disease prevention, and individualised care.

Nevertheless, this thesis acknowledges limitations, notably excluding COVID-19 from the analysis. While this focus allowed for a detailed exploration of other VPDs, integrating data

on the impact of the COVID-19 pandemic could offer a deeper understanding of the current trends in travel medicine. The pandemic has emphasised the need for dynamic public health strategies that can rapidly adapt to pandemics, especially in the context of global travel. Moreover, while the case study outlines proactive measures like malaria prophylaxis and standby treatment for traveller's diarrhoea, broader data on adherence rates would enhance the significance of the preventions. For instance, the literature review reveals that vaccines like Hepatitis A and Yellow Fever show effectiveness rates of over 95%, yet adherence varies significantly across traveller populations. (59)

While individual vaccination protocols are crucial, it is equally important to consider the broader implications of these practices through an epidemiological lens, as demonstrated by the contrasting public health strategies of Lithuania and the U.S. The analysis reveals the complexities and nuances of public health strategies tailored to the local epidemiological situation. Lithuania's implementation of the BCG vaccine at birth is not just a preventive measure but a critical response to its significantly higher T.B. incidence compared to the U.S. This choice underscores a principle in vaccination policies; the importance of aligning public health actions with specific health landscape realities, which might not be immediately evident without considering underlying epidemiological data.

Conversely, the U.S. strategy of universally vaccinating against varicella and influenza demonstrates a proactive stance in preventing widespread outbreaks and managing diseases with potentially high morbidity and mortality in larger, diverse populations. Although these approaches appear more comprehensive, they also bring attention to challenges related to cost-effectiveness and public compliance—issues that Lithuania might approach differently based on its resources and disease prevalence.

To advance travel medicine, future research should investigate the impact of novel vaccine technologies, such as mRNA vaccines for malaria and Zika, which promise to revolutionise travel medicine by offering more robust protection against these diseases.(60) Additionally, investigating innovative mosquito control and eradication methods could significantly reduce the transmission of mosquito-borne diseases. The potential for genetic modification strategies or novel biological control methods is exciting and warrants further exploration to enhance travel health safety.(61) Lastly, comprehensive studies are needed to compare the effectiveness of pre-travel consultations in enhancing adherence to vaccination and preventive measures. Such research could provide evidence for global policy adjustments and improved educational strategies to boost compliance and safe travel practices.

10. CONCLUSION

This thesis affirms that vaccinations and pre-travel consultations are cornerstones of travel medicine, essential for protecting travellers from vaccine-preventable diseases. It emphasises the importance of individualised, evidence-based practices while highlighting the complex nature of health problems in travel, which depend on factors such as the traveller's age, the nature of the trip, and other specific conditions.

The work acknowledges that vaccination recommendations can vary widely, underscoring clinicians' need to adapt prevention strategies to each traveller's specific epidemiological contexts. This ensures that approaches are customised to the unique risks associated with international travel. Such a differentiated approach is essential not only to manage the impact of travel on travellers' health but also to effectively reduce the global burden of vaccine-preventable diseases.

By analysing different public health systems and underscoring the need for better adherence and innovative research, this thesis contributes to a deeper understanding of optimally preparing travellers. Future research and public health initiatives must continue refining these strategies, ensuring travellers are well-prepared to explore the world safely and responsibly, thereby strengthening public health locally and internationally.

11. LIST OF REFERENCES

1. Smallpox: Variolation [Internet]. U.S. National Library of Medicine; [cited 2024 Apr 9]. Available from: https://www.nlm.nih.gov/exhibition/smallpox/sp_variolation.html

2. A Brief History of Vaccination [Internet]. [cited 2024 Apr 9]. Available from: https://www.who.int/news-room/spotlight/history-of-vaccination/a-brief-history-of-vaccination

3. Immunization coverage [Internet]. [cited 2024 Apr 9]. Available from: https://www.who.int/news-room/fact-sheets/detail/immunization-coverage

4. Carter A, Msemburi W, Sim SY, A.M. Gaythorpe K, Lindstrand A, Hutubessy RCW. Modeling the Impact of Vaccination for the Immunization Agenda 2030: Deaths Averted Due to Vaccination Against 14 Pathogens in 194 Countries from 2021-2030. SSRN Electron J [Internet]. 2021 [cited 2024 Apr 25]; Available from: https://www.ssrn.com/abstract=3830781

5. Pollard AJ, Bijker EM. A guide to vaccinology: from basic principles to new developments. Nat Rev Immunol. 2021 Feb;21(2):83–100.

6. Murthy N, Wodi AP, McNally VV, Daley MF, Cineas S, Advisory Committee on Immunization Practices. Recommended Adult Immunization Schedule, United States, 2024. Ann Intern Med. 2024 Feb 20;177(2):221–37.

7. About Diphtheria, Tetanus, and Pertussis Vaccination | CDC [Internet]. 2024 [cited 2024 Apr 30]. Available from: https://www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/about-vaccine.html

8. Paget J, Spreeuwenberg P, Charu V, Taylor RJ, Iuliano AD, Bresee J, et al. Global mortality associated with seasonal influenza epidemics: New burden estimates and predictors from the GLaMOR Project. J Glob Health. 9(2):020421.

9. Nuwarda RF, Alharbi AA, Kayser V. An Overview of Influenza Viruses and Vaccines. Vaccines. 2021 Sep 17;9(9):1032.

10. Recommended composition of influenza virus vaccines for use in the 2023 southern hemisphere influenza season [Internet]. [cited 2024 Apr 23]. Available from: https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2023-southern-hemisphere-influenza-season

11. Davies HG, Bowman C, Luby SP. Cholera – management and prevention. J Infect. 2017 Jun 1;74:S66–73.

12. Cholera | CDC Yellow Book 2024 [Internet]. [cited 2024 Apr 17]. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/cholera#diagnosis

13. Ilic I, Ilic M. Global Patterns of Trends in Cholera Mortality. Trop Med Infect Dis. 2023 Mar 13;8(3):169.

14. Abutaleb A, Kottilil S. Hepatitis A. Gastroenterol Clin North Am. 2020 Jun;49(2):191–9.

15. who-surveillancevaccinepreventable-06-hepa-r2.pdf [Internet]. [cited 2024 Apr 30]. Available from: https://cdn.who.int/media/docs/default-source/immunization/vpd_surveillance/vpd-surveillance-standards-publication/who-surveillancevaccinepreventable-06-hepa-r2.pdf?sfvrsn=8560530_10&download=true

16. Pinkbook: Hepatitis A | CDC [Internet]. 2023 [cited 2024 May 9]. Available from: https://www.cdc.gov/vaccines/pubs/pinkbook/hepa.html

17. Park SL, Huang YJS, Vanlandingham DL. Re-Examining the Importance of Pigs in the Transmission of Japanese Encephalitis Virus. Pathogens. 2022 May 13;11(5):575.

18. Simon LV, Sandhu DS, Goyal A, Kruse B. Japanese Encephalitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Apr 18]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK470423/

19. Symptoms & Treatment | Japanese Encephalitis | CDC [Internet]. 2023 [cited 2024 Apr 18]. Available from: https://www.cdc.gov/japaneseencephalitis/symptoms/index.html

20. ixiaro-epar-medicine-overview_en.pdf [Internet]. [cited 2024 Apr 18]. Available from: https://www.ema.europa.eu/en/documents/overview/ixiaro-epar-medicine-overview_en.pdf

21. Parikh SR, Campbell H, Bettinger JA, Harrison LH, Marshall HS, Martinon-Torres F, et al. The everchanging epidemiology of meningococcal disease worldwide and the potential for prevention through vaccination. J Infect. 2020 Oct;81(4):483–98.

22. Stellungnahme der Ständigen Impfkommission (STIKO) am Robert Koch-Institut (RKI) zum Stand der Bewertung des neuen Meningokokken-B-Impfstoffs Bexsero®. Krankenh-Hyg Infekt. 2014 Mar;36(1):40.

23. Pinkbook: Poliomyelitis | CDC [Internet]. 2023 [cited 2024 May 1]. Available from: https://www.cdc.gov/vaccines/pubs/pinkbook/polio.html

24. Patel PD, Liang Y, Meiring JE, Chasweka N, Patel P, Misiri T, et al. Efficacy of typhoid conjugate vaccine: final analysis of a 4-year, phase 3, randomised controlled trial in Malawian children. The Lancet. 2024 Feb 3;403(10425):459–68.

25. Zero by 30 | Rabies - Bulletin - Europe [Internet]. [cited 2024 Apr 15]. Available from: https://www.who-rabies-bulletin.org/site-page/zero-30

26. Worku DA. Tick-Borne Encephalitis (TBE): From Tick to Pathology. J Clin Med. 2023 Oct 30;12(21):6859.

27. Pustijanac E, Buršić M, Talapko J, Škrlec I, Meštrović T, Lišnjić D. Tick-Borne Encephalitis Virus: A Comprehensive Review of Transmission, Pathogenesis, Epidemiology, Clinical Manifestations, Diagnosis, and Prevention. Microorganisms. 2023 Jun 22;11(7):1634.

28. GPEI-Polio Today [Internet]. [cited 2024 May 4]. Available from: https://polioeradication.org/polio-today/

29. Angelo KM, Kozarsky PE, Ryan ET, Chen LH, Sotir MJ. What proportion of international travellers acquire a travel-related illness? A review of the literature. J Travel Med. 2017 Sep 1;24(5):10.1093/jtm/tax046.

30. Matsee W, Charoensakulchai S, Khatib AN. Heat-related illnesses are an increasing threat for travellers to hot climate destinations. J Travel Med. 2023 May 24;30(4):taad072.

31. Peng ZY, He MZ, Zhou LY, Wu XY, Wang LM, Li N, et al. Mosquito Repellents: Efficacy Tests of Commercial Skin-Applied Products in China. Molecules. 2022 Aug 28;27(17):5534.

32. Epidemic Diseases - Yellow Fever in the Americas [Internet]. [cited 2024 Apr 28]. Available from: https://ais.paho.org/phip/viz/ed_yellowfever.asp

33. Yellow fever, the returning epidemic - PAHO/WHO | Pan American Health Organization [Internet]. [cited 2024 Apr 28]. Available from: https://www.paho.org/en/stories/yellow-fever-returning-epidemic

34. Malaria - PAHO/WHO | Pan American Health Organization [Internet]. 2024 [cited 2024 May 4]. Available from: https://www.paho.org/en/topics/malaria

35. Prevent Mosquito Bites | Mosquitoes | CDC [Internet]. 2023 [cited 2024 Apr 28]. Available from: https://www.cdc.gov/mosquitoes/mosquito-bites/prevent-mosquito-bites.html

36. Ly H. Ixchiq (VLA1553): The first FDA-approved vaccine to prevent disease caused by Chikungunya virus infection. Virulence. 15(1):2301573.

37. ACIP Vaccine Recommendations and Schedules | CDC [Internet]. 2024 [cited 2024 Apr 28]. Available from: https://www.cdc.gov/vaccines/acip/recommendations.html

38. Satterfield-Nash A, Kotzky K, Allen J, Bertolli J, Moore CA, Pereira IO, et al. Health and Development at Age 19–24 Months of 19 Children Who Were Born with Microcephaly and Laboratory Evidence of Congenital Zika Virus Infection During the 2015 Zika Virus Outbreak — Brazil, 2017. Morb Mortal Wkly Rep. 2017 Dec 15;66(49):1347–51.

39. Leptospirosis | CDC Yellow Book 2024 [Internet]. [cited 2024 Apr 28]. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/leptospirosis#prevent

40. Luks AM, Swenson ER, Bärtsch P. Acute high-altitude sickness. Eur Respir Rev. 2017 Feb 1;26(143):160096.

41. Qureshi AI, editor. Chapter 2 - Mosquito-Borne Diseases. In: Zika Virus Disease [Internet]. Academic Press; 2018 [cited 2024 Apr 29]. p. 27–45. Available from: https://www.sciencedirect.com/science/article/pii/B9780128123652000032

42. Hasler T, Fehr J, Held U, Schlagenhauf P. Use of repellents by travellers: A randomised, quantitative analysis of applied dosage and an evaluation of knowledge, Attitudes and Practices (KAP). Travel Med Infect Dis. 2019;28:27–33.

43. Insect Repellents Fact Sheet [Internet]. [cited 2024 Apr 29]. Available from: http://npic.orst.edu/factsheets/repellents.html#refs

44. Percutaneous penetration and pharmacodynamics: Wash-in and wash-off of sunscreen and insect repellent [Internet]. [cited 2024 Apr 29]. Available from: https://www.tandfonline.com/doi/epdf/10.3109/09546634.2015.1050350?needAccess=true

45. Orsborne J, DeRaedt Banks S, Hendy A, Gezan SA, Kaur H, Wilder-Smith A, et al. Personal Protection of Permethrin-Treated Clothing against Aedes aegypti, the Vector of Dengue and Zika Virus, in the Laboratory. PLoS ONE. 2016 May 17;11(5):e0152805.

46. Maia MF, Kliner M, Richardson M, Lengeler C, Moore SJ. Mosquito repellents for malaria prevention. Cochrane Database Syst Rev. 2018 Feb 6;2018(2):CD011595.

47. Yang G geun, Kim D, Pham A, Paul CJ. A Meta-Regression Analysis of the Effectiveness of Mosquito Nets for Malaria Control: The Value of Long-Lasting Insecticide Nets. Int J Environ Res Public Health. 2018 Mar;15(3):546.

48. Zoonotic Exposures: Bites, Stings, Scratches & Other Hazards | CDC Yellow Book 2024 [Internet]. [cited 2024 Apr 29]. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2024/environmental-hazards-risks/zoonotic-exposures-bites-stings-scratches-and-other-hazards

49. Longbottom J, Shearer FM, Devine M, Alcoba G, Chappuis F, Weiss DJ, et al. Vulnerability to snakebite envenoming: a global mapping of hotspots. Lancet Lond Engl. 2018 Aug 25;392(10148):673–84.

50. Travelers' Diarrhea | CDC Yellow Book 2024 [Internet]. [cited 2024 Apr 29]. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/travelers-diarrhea

51. Cohen A, Colford JM. Effects of Boiling Drinking Water on Diarrhea and Pathogen-Specific Infections in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Am J Trop Med Hyg. 2017 Nov 8;97(5):1362–77.

52. Water Disinfection | CDC Yellow Book 2024 [Internet]. [cited 2024 Apr 29]. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/water-disinfection

53. Zarembaitė G, Žiūkaitė G, Chmieliauskas S, Vasiljevaitė D, Laima S, Stasiūnienė J. Tuberculosis and Sudden Death in Lithuania. Acta Medica Litu. 2023;30(2):152–62.

54. CDCTB. Centers for Disease Control and Prevention. 2023 [cited 2024 May 2]. Reported TB in the U.S., 2021- National Data. Available from: https://www.cdc.gov/tb/statistics/reports/2022/national_data.htm

55. Marin M, Seward JF, Gershon AA. 25 Years of Varicella Vaccination in the United States. J Infect Dis. 2022 Oct 21;226(Suppl 4):S375–9.

56. Chickenpox Is an Extremely Contagious Disease but Can Be Avoided by Vaccination [Internet]. [cited 2024 May 9]. Available from: https://nvsc.lrv.lt/en/naujienos/chickenpox-is-an-extremely-contagious-disease-but-can-be-avoided-by-vaccination/

57. Pawaskar M, Méroc E, Samant S, Flem E, Bencina G, Riera-Montes M, et al. Economic burden of varicella in Europe in the absence of universal varicella vaccination. BMC Public Health. 2021 Dec 21;21:2312.

58. Vlot JA, Vive MGD, Brockhoff HJ, van Genderen PJJ, Trompenaars MCE, van Steenbergen JE, et al. Predicting morbidity in older travellers during a short-term stay in the tropics: the ELDEST study. J Travel Med. 2020 Nov 19;28(1):taaa216.

59. Kwon HY, Lee H, Im JH, Park SG, Lee YJ, Baek JH, et al. Determinants of Compliance of Travelers with Vaccination and Malaria Prophylaxis at a Travel Clinic. J Korean Med Sci. 2019 Aug 26;34(33):e217.

60. Essink B, Chu L, Seger W, Barranco E, Le Cam N, Bennett H, et al. The safety and immunogenicity of two Zika virus mRNA vaccine candidates in healthy flavivirus baseline seropositive and seronegative adults: the results of two randomised, placebo-controlled, dose-ranging, phase 1 clinical trials. Lancet Infect Dis. 2023 May;23(5):621–33.

61. Powell JR. Modifying mosquitoes to suppress disease transmission: Is the long wait over? Genetics. 2022 Jun 2;221(3):iyac072.

Annex 6. Pledge. To be completed by the student when uploading the thesis to the VUSIS; no separate submission of the pledge is required

Vilniaus universiteto studento, teikiančio baigiamąjį darbą, GARANTIJA	**PLEDGE of Vilnius University student submitting a thesis**
Vardas ir pavardė:	Given name and surname: Darwin Ghafar Rahim
Padalinys:	Faculty: Faculty of medicine
Studijų programa:	Study programme: Medicine, Integrated studies
Darbo pavadinimas:	Thesis topic:
Darbo tipas:	Vaccination of Travelers: Case Presentation, Vaccine-Preventable Travel Health Risks and Comparison of Vaccination Recommendations in Europe and the US Thesis type: Literature Review
Garantuoju, kad mano baigiamasis darbas yra parengtas sąžiningai ir savarankiškai, kitų asmenų indėlio į parengtą darbą nėra. Jokio neteisėto atlygio už šį darbą niekam nesu mokėjęs. Šiame darbe tiesiogiai ar netiesiogiai panaudotos kitų šaltinių citatos pažymėtos literatūros nuorodose.	I pledge that my thesis has been prepared in good faith and independently and that there has been no contribution by other individuals to this thesis. I have not made any illegal payments related to this thesis. Quotes from other sources used in this thesis, directly or indirectly, are indicated in the list of references.
Aš, [Vardas Pavardė], patvirtinu (pažymėti) ☐	I, Darwin Ghafar Rahim, *confirm (check)* ☑

Patvirtinu, kad baigiamasis darbas yra įkeltas į Vilniaus universiteto studijų informacinę sistemą.

I declare that this thesis has been uploaded to the Vilnius University Study Information System.

Darwin Ghafar Rahim	D.Rahim	2024.05.10
(vardas ir pavardė / *given name and surname*)	(parašas / *signature*)	(data / *date*)

Embargo laikotarpis / *Embargo period*

Prašau nustatyti šiam baigiamajam darbui toliau nurodytos trukmės embargo laikotarpį:

I am requesting an embargo on this thesis for the period indicated below:

☐ _____ mėnesių / months [embargo laikotarpis negali viršyti 60 mėn. / *an embargo period cannot not exceed 60 months*];

☑ embargo laikotarpis nereikalingas / *no embargo period is requested.*

Embargo laikotarpio nustatymo priežastis / *reason for the embargo period*:

.....

Darwin Ghafar Rahim		2024.05.10
(vardas ir pavardė / *given name and surname*)	(parašas / *signature*)	(data / *date*)

Padalinio administratoriaus patvirtinimas, kad baigiamasis darbas buvo pateiktas ir užregistruotas / *Confirmation from the unit administrator that the thesis has been submitted and registered*:

(vardas ir pavardė / *given name and surname*)	(parašas / *signature*)	(data / *date*)