

ambulatory services while abroad, 61% utilized outpatient services at home. Each dengue episode resulted in a median loss of 10 (IQR 6 – 15) work or school days, each malaria episode a median loss of 5 (IQR 3 – 7) days, each chikungunya episode a median loss of 7 (IQR 6 – 9) days, and each Zika virus episode a median loss of 7 (IQR 4 – 9) days. The average direct out-of-pocket hospitalization cost in the destination country (US\$2,236; range: \$108-\$5,160) was significantly higher than the direct out-of-pocket ambulatory cost in the destination country (US\$327; range: \$0-\$1,560), the direct out-of-pocket hospitalization cost in the home country (US\$35; range: \$0-\$120), and the direct out-of-pocket ambulatory costs in the home country (US\$45; range: \$0-\$192). Respondents with dengue or malaria lost a median of USD \$570 (IQR 240 – 1140) and USD \$240 (IQR 0 – 600), respectively, due to their illness, while those with chikungunya and Zika virus lost a median of USD \$2,400 (IQR 1200 – 3600) and USD \$1,500 (IQR 510 – 2625), respectively.

**Conclusions:** Travelers often incur significant costs due to travel-acquired diseases. Further research into the economic impact of these diseases on travelers should be conducted.

**Conflict of Interest:** None

**previously\_presented:** ASTMH 2022 in Seattle, USA (Poster ppt)

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### **Trials and Tribulations of Conducting RCTs in Mass Gatherings**

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**Background:** Limited number of randomised controlled trials (RCTs) have been conducted in the field of travel medicine. Mass gatherings (MGs) such as Hajj pilgrimage provide a unique opportunity to conduct RCTs that require a large sample size but are often fraught with various challenges. Here we describe the challenges we faced while conducting RCTs at MGs.

**Objectives:** To present the challenges we faced while conducting RCTs at MGs.

**Methods:** This is a qualitative description of various challenges we encountered during the execution of six RCTs (including pilot trials) at Hajj and Umrah MGs conducted from 2011 to 2021. We focus on the challenges or setbacks experienced by investigators, data collectors and participants, and discuss the difficulties experienced during logistic operation and field work.

**Results:** From 2011 to 2021, we conducted six RCTs including two pilot RCTs, all but one involving Hajj pilgrims from Australia, Saudi Arabia and Qatar, and the other involved Umrah pilgrims from Saudi Arabia. These RCTs explored the effect of facemask or hand hygiene against respiratory viral infections, immunological interactions of vaccines, and the effect of conjugate vaccines on pharyngeal bacterial carriage. The challenges experienced are related to: a) collaboration, b) logistics, c) trial execution, d) data quality, and e) funding. Challenges of collaboration include poor cooperation, not meeting deadlines and changing mind at the last minute. Logistic issues include unavailability or delay in the supply of study tools, products, diagnostics and maintenance of cold chain. Issues with the execution of RCTs include randomisation, blinding, inadequate follow-up, and importantly poor compliance of the trial participants. Issues with data quality include submission of incomplete questionnaires, loss to follow up, suboptimal training or performance of the data collectors. Funding issues include non-release of grant money before the start of field work, and withdrawal of funding due to regional political crises.

**Conclusions:** There are preventable challenges in conducting RCTs in MGs.

**Conflict of Interest:** Nil.

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### **A Systematic Review of Treatment Strategies for Percutaneously Introduced Marine Toxins and Venom**

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**Background:** Marine envenomation's are common worldwide, and can range from mild to severe, the latter causing a multitude of symptoms including paralysis, cardiac depression and neurological toxicity. Without appropriate medical intervention, marine envenomation's can be fatal. With the rising prevalence of travel and ecotourism, potential exists for increased exposure to marine stings and penetrating marine injuries.

**Objectives:** We aim to synthesize existing evidence around diagnosis, treatment and prevention of marine envenomation's into a clinical resource.

**Methods:** Four electronic databases were searched from inception to August 2019 using combinations of the search terms "marine", and "envenomation." Iterative inclusion and exclusion of search terms were employed to maximize article extraction. The search was refined to humans only, without language restriction. For the systematic review, we will include observational studies, case reports, case series, and cohort studies, as well as clinical trials, and therapeutics tolerability and efficacy. The GRADE approach will be employed to assess quality of studies reporting therapeutic interventions. Evidence will be summarized using descriptive measures for each intervention type. Meta-analysis will be planned if sufficient efficacy measures exist.

**Results:** 299 MEDLINE articles, 1060 PubMed, 937 EMBASE, and 1785 BioSIS records were retrieved for title and abstract screening. Of those, 1152 duplicates were removed, with 2926 remaining and 266 from LILACS. Data will be grouped and summarized for ease of clinician use by marine organism, syndrome, prevention and therapeutic strategies, and according to geographic location and species. Thus far in our search, *jellyfish* (47), *scorpaenidae* (24), and *stingrays* (21) are the leading etiological agents for marine envenomation's. Also, the geographical areas of interest for the envenomation's included North America (30 total envenomation's), Europe (22 total envenomation's), and Australia (13 total envenomation's).

**Conclusions:** With increased globalization, as well as the rising numbers of clinicians electing to train or work in areas where marine envenomation's are common, it is important to synthesize the current evidence around clinical epidemiology, presentation and management for marine envenomation's. This synthesis will subsequently help to develop updated public health protocols to ensure timely and effective medical intervention for marine envenomation's.

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### **Safety and Immunogenicity of an Investigational Yellow Fever Vaccine in Adults**

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**Background:** The re-emergence of yellow fever (YF) as a global threat to public health and the recent shortages of licensed vaccines in the face of multiple regional outbreaks has underscored the need for newer YF vaccines that match currently available products in safety and effectiveness, but improve upon ease of manufacturing. vYF is a next-generation live-attenuated YF vaccine grown in serum-free Vero cells, developed to ensure more sustainable and robust supply. Preclinical testing of vYF demonstrated equivalence to licensed YF vaccines. In a Phase I clinical trial in adults (UTN: U1111-1217-1958), vYF was shown to be safe at all tested doses and to elicit a protective immune response.

**Objectives:** We conducted a Phase II randomized, observer-blind, active-controlled (YF-VAX), non-inferiority multicenter study of vYF, 5Log CCID<sub>50</sub>/dose, in 18–60-year-old adults, in the USA (BB-IND: IND #: 019167; WHO UTN: U1111-1261-5612).

**Methods:** 565 adults were randomized 2:1 to receive vYF or YF-VAX. Solicited and unsolicited adverse events (AE) were collected in all participants, hematologic and biochemical parameters