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# Aggregate travel vs. single trip assessment: Arguments for cumulative risk analysis

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ABSTRACT

Vaccine recommendations for travellers are based on individual risk assessments of multiple factors, most importantly the destination and duration of the impending trip. Many people undertake frequent trips, but existing WHO, CDC and national advisory board recommendations do not explicitly consider cumulative travel-associated risks. Given the period of protection provided by many vaccines, in particular rabies, hepatitis A, hepatitis B and yellow fever vaccines, an aggregate multi-trip risk assessment which views vaccines as an investment for future travel health may be more appropriate than separately evaluating the risks for each trip.



Recommendations about whether or not to vaccinate travellers before their trip are typically made on the basis of an individual risk-benefit assessment and cost considerations. The risk assessment takes into account the epidemiology of the disease in the area to be visited, risk factors related to the particular itinerary and host, duration of travel, severity and treatability of the disease, and the efficacy and adverse events associated with the vaccine. Of these factors, trip duration is often a critical factor, with guidelines for certain vaccines being dependent on the expected duration of exposure during the imminent trip.

A subset of travellers visit developing countries frequently, some because of interest, some to visit friends or relatives, and some related to business. However, additional periods of exposure during future trips and during the timeframe of protection afforded by specific vaccines are not usually formally incorporated into the pre-travel risk assessment. Some impending travellers may volunteer that they are planning future travel and some travel medicine practitioners may ask about the possibility of future travel when making decisions about pre-travel needs, but there is currently no explicit consideration given in WHO [1] or CDC [2] guidelines or in national advisory board recommendations to the cumulative travel-associated risks from future trips, even though this makes intuitive sense.

Box: Examples of traveller characteristics that favour the cumulative travel risk assessment approach
- Frequent international travel
  - Corporate traveller
  - Nonprofit organization staff
  - Airline crew
- Open itinerary
  - Backpacker
  - Budget traveller
  - Past travel with open itinerary
- Anticipate last minute travel
  - Humanitarian and emergency relief workers
  - Military or contract personnel personnel
- Anticipate repeat travel
  - Visiting friends and relatives (VFR)
  - Missionaries

The standard approach of considering exposure risks only in terms of the upcoming trip is the logical approach for a disease such as malaria, with the length of stay in a malaria transmission area and the transmission intensity for the impending trip being the relevant factors to balance against chemoprophylaxis issues. However, unlike malaria prophylaxis, many vaccines provide long-term protection, some affording life-long protection (Fig. 1). Therefore, considering only the upcoming trip when making decisions regarding the need for and cost-effectiveness of vaccination is

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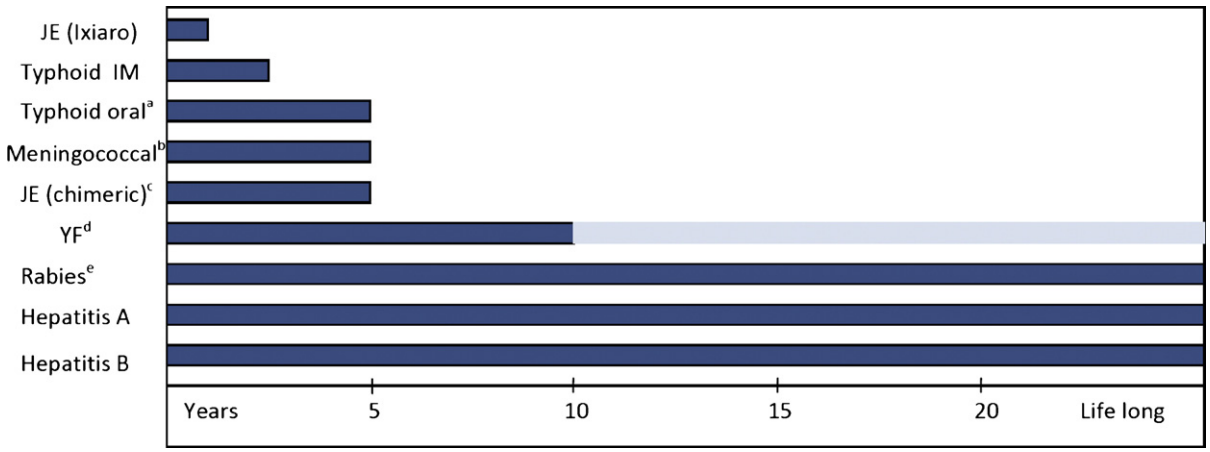


**Fig. 1.** Vaccines and estimated duration of protection (after complete, primary series). *Note*: some vaccines are region specific (JE, YF); other vaccines are relevant broadly for travel to developing regions of the world (e.g., hepatitis A, hepatitis B, rabies). [a]4-dose oral schedule. [b]Conjugate meningococcal vaccine. [c]Anticipated duration of protection (studies in progress). [d]YF vaccination certificate is valid for 10 years, though immunologic protection is longer than this in most individuals. [e]Booster doses with rabies vaccine are needed in the event of rabies exposure, but RIG is not needed once a full vaccination course has been received. Hepatitis A and Hepatitis B are presumed to provide life-long protection.

questionable. Even if the risk to the individual traveller from a single trip is low, many infections for which vaccines are recommended are expected to continue to pose risks to travellers during subsequent trips.

If future travel were incorporated into the risk equation, the decision regarding vaccination might change. Therefore should vaccination be regarded as an investment, rather than having its value assessed just in terms of the impending trip? And should the likelihood of future trips be formally incorporated into the pre-travel risk assessment? Depending on the duration of protection from an individual vaccine, the decision regarding vaccination could be based on the concept of a 2-year, 3-year, 5-year or lifetime risk assessment, rather than on an individual trip risk evaluation (Table 1). This opportunistic approach to vaccination may provide ongoing health benefits for future trips, and additionally may benefit the individual by protecting them in their country of residence.

Consideration of an aggregate exposure risk assessment for travel vaccines is consistent with the concepts used for recommending routine childhood vaccines, for which both current and future benefits are considered, even though in the travel context a targeted rather than universal approach is used. Based on data obtained from an internet-based cross sectional survey of Danes, Nielsen and colleagues estimated the cumulative lifetime stay in hepatitis B-endemic areas outside Europe was 4.3 months [3]. Over 93% of US outbound travellers in 2009 were making repeat international trips; the travellers took a mean of 2.4 trips in the previous 12 months, and 9.2 trips in the previous 5 years [4]. There may not always be a linear association between risk and travel length, and the risk of four 1-week trips may not be the same as one 4-week trip for all diseases, but it provides a general approximation and this approach of considering vaccination as an investment for future travel health is nevertheless appropriate.

A clear advantage of considering the cumulative risk approach is that previous vaccination would avoid many of the potential problems associated with last minute travel, uncertainty with travel plans, and changes to itineraries. It is also pertinent for organizations that have a preference for efficiency in preparations, such as the military, where persons must be prepared for wide "travel". Other groups for whom this approach may be particularly appropriate include airline pilots and flight attendants, staff of multinational organizations who need to travel frequently and globally, people working with nonprofit organizations, and those involved in emergency relief efforts. Individuals or families who are travelling to visit friends and relatives in developing countries have been identified in multiple studies as being at increased risk for many travel-associated infections, including some that are vaccine preventable, such as typhoid fever [5–7]. Many of them travel annually or regularly to visit family, and therefore would also be appropriate targets for evaluation using an aggregate exposure framework. This approach may mean that younger travellers are especially good candidates for vaccination purely on an age basis since they will have many opportunities for aggregating prolonged exposure. Increasing the likelihood that travellers are vaccinated when they are young and healthy has an added advantage as the elderly may have lower seroconversion rates and/or greater risk of adverse events following immunisation [8–10].

## 1. Relevance of cumulative travel risk analysis to specific vaccines

### 1.1. Rabies vaccine

The interventions for which this approach would be especially relevant would be vaccines with long lasting protection and a good safety profile, especially if they also have high expense. Perhaps the most pertinent example is rabies vaccination. Travellers seeking care for animal related exposures frequently have severe injuries (e.g., WHO category III wounds for which human rabies immune globulin (hRIG) and rabies vaccine are recommended [11,12]). Rabies post-exposure treatment that includes hRIG and tissue culture vaccine is safe and highly efficacious if given promptly after exposure to a potentially rabid animal. In reality, however, hRIG is unavailable in many of the regions where rabies is endemic, rabies vaccines vary in quality and safety, and good medical care may not be accessible locally. Therefore the treatment given is frequently incorrect, incomplete, or delayed, or treatment is omitted entirely. Additionally, travellers are often unaware of the risk of exposure and the need to receive post exposure treatment. Among French travellers, for example, only 6.7% knew that rabies was important [13]. Among backpackers in Bangkok, 37% did not know that cats can carry rabies; 41% were unaware that a lick to broken skin was a risk [14].

The risk of bite exposures during travel varies with activities and by region of travel. In a GeoSentinel study, 67% of bite exposures occurred in Asia (top countries: Thailand, India, Indonesia, China, Nepal, Vietnam) [15]. Additionally, travel duration (e.g., >1 month) is sometimes used to help inform the priority that should be given to pre-exposure rabies vaccination for individual travellers.