



Published in final edited form as:

J Travel Med. 2025 November 23; 32(7): . doi:10.1093/jtm/taaf053.

Economic value of pre-travel health interventions for communicable diseases in international travellers

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Abstract

Background: Pre-travel health interventions can reduce the acquisition of communicable diseases and decrease the risk of transmission during or after international travel. We sought to inform policy and research priorities with a scoping literature review of studies that assess the cost-effectiveness of pre-travel interventions.

Methods: We assessed 44 economic evaluation studies published from 1946–2023, regarding pre-travel prevention of hepatitis A, hepatitis B, influenza, malaria, rabies, travellers' diarrhoea, cholera, polio, typhoid fever, measles, and Japanese encephalitis.

Results: Published studies demonstrate that hepatitis A vaccination, malaria chemoprophylaxis and typhoid vaccination for people travelling to highly endemic settings are likely to be cost-effective, as is measles-mumps-rubella vaccination. The cost-effectiveness of other pre-travel interventions is more sensitive to travel frequency and duration, endemicity at the travel

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Conflict of interest

The authors have declared that no conflicts of interest exist.

destination, travel purpose (e.g. business, leisure, visiting friends and relatives), risk perceptions (e.g. adherence to care plan, choosing to vaccinate), and costs.

Conclusions: Cost-effectiveness analyses of pre-travel interventions can inform the value of such interventions, but such analyses depend on the availability of high-quality data regarding clinical outcomes and costs. We propose that international, collaborative networks should collect data and leverage novel technologies to expand the evidence base regarding the risks of exposure, clinical outcomes, risk perception, and costs associated with pre-travel interventions. This evidence base can inform recommendations for specific groups of travellers and the formulation of population-specific health policies.

Keywords

Pre-travel health intervention; cost-effectiveness; communicable diseases

Introduction

International travel increases the risk of communicable diseases, which results in individual illness and can provoke outbreaks, epidemics, and pandemics. More than one billion international border crossings occurred in 2023 alone, and international travel increased forty-fold between 1950 and 2023.^{1,2} International air travel, which enables the rapid global movement of people, has been steadily growing with the total number of passengers using air travel rising to 3.3 billion in 2023.^{3,4} Although the COVID-19 pandemic sharply curtailed international travel with travel restrictions endorsed by every country worldwide by April 2020,³ international travel has since resumed and will continue to grow.⁵ The COVID-19 pandemic, as well as the 2025 measles outbreak in the US, have emphasized the role of international travel in the geographic spread of communicable diseases and highlights the need to invest in pre-travel health preparation.

To mitigate these risks, the Centers for Disease Control and Prevention provides destination-specific health advice.⁶ Pre-travel health consultations draw on these recommendations to provide preventive counselling to travellers and offer prophylactic medications and immunizations. Such consultations can reduce the risks of communicable diseases due to international travel and provide important health benefits with costs incurred by the traveller and healthcare system.⁶ Although published analyses have evaluated the benefits and costs of selected pre-travel health interventions, no comprehensive analysis of the existing clinical and economic evidence for pre-travel health consultations has been performed.

We present a scoping review of published cost-effectiveness analyses of pre-travel interventions for communicable diseases. We critically assessed each study and summarized outcomes to inform future research and policy on interventions to prevent travel-associated communicable diseases.

Methods

Data sources and search strategy

We used free text terms to search for articles indexed in the PubMed database from January 1946 to January 2024. Search term combinations paired each of cost–benefit, cost-utility, cost-effectiveness, and cost with the following terms: hepatitis A, hepatitis B, influenza, malaria, rabies, traveller’s diarrhoea, cholera, polio, typhoid fever, measles, Japanese encephalitis, yellow fever, meningococcal disease, tetanus and varicella. The terms, ‘vaccine’ and ‘travel,’ were also added to the disease-containing combinations. We manually searched the bibliographies of eligible articles to identify other articles of interest. We conducted a scoping search of articles using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist and reporting recommendations.⁷ The complete search strategy is available as Supplementary Appendix 1.

Eligibility criteria and study selection

For all articles that included the words ‘cost’ or a travel-related term (i.e. ‘travel,’ ‘tourist/sm’ or ‘deploy’) within the abstract or title, reviewers (TS, NFF, NMM, SK or EPH) then independently evaluated the abstracts according to pre-specified criteria: population (travellers), study design (cost-effectiveness, cost–benefit, cost-utility analysis or cost-comparison analysis), intervention (a pre-travel medical screening or provision of prophylaxis for a travel-related disease) and outcomes (clinical outcomes, costs, and cost-effectiveness results). Among abstracts that met inclusion criteria, full-text review was performed; we included articles for data abstraction, if consensus was reached among the reviewers (SK and EPH) during discussion after independent review of the articles’ full text.

We assessed cost-effectiveness analyses (comparison of interventions as costs per clinical outcome, including quality-adjusted life years [QALYs]), cost–benefit analyses (comparison of costs and benefits of interventions quantified by costs), cost-minimization analyses (comparisons of cost estimations for different interventions with the same efficacy).^{8,9} We excluded studies that were review or opinion articles, presented only primary data collection, evaluated clinical benefits only, were not in English, or only assessed diseases rarely reported among travellers (e.g. anthrax, diphtheria, mumps, pertussis, pneumococcal disease and rubella).

Data extraction

We generated a data abstraction procedure (Supplementary Appendix 2).¹⁰ Data elements included the methods, input parameters, outcomes, sensitivity analyses, limitations, and conclusions. Two reviewers abstracted all data individually (TS, NFF or SK), with differences adjudicated by a third reviewer (EPH).

Results

Article selection

A search of PubMed yielded a total of 42100 articles as of January 2024 (Fig. 1). Following the removal of duplicates, 20749 articles remained, and we excluded 20083 articles because

the terms ‘costs’ and a travel-related term (‘travel,’ ‘tourist/sm’) or ‘deploy’) were not included in the title or abstract. We next screened the remaining 666 articles by reviewing their abstracts and excluded 600 articles because the abstracts were: not about pre-travel interventions (n=151), a review article or opinion article or case report or guidelines or book (n=71), without cost assessment (n=69), not about travellers (n=298), presented only primary data (n=8) or not written in English (n=3). Upon review of the full text of the remaining 66 articles, we excluded 22 additional articles (i.e. were not analyses in scope, were review articles, not about travellers, included benefits only, or not about pre-travel interventions). Therefore, we included 44 articles published from 1988 to 2022 in this review (Fig. 2).^{11–52}

Overview

Table 1 provides an overview of the 44 articles included in this scoping review. Seventeen (39%) articles analysed pre-travel interventions for hepatitis A, and six articles were for travellers’ diarrhoea, followed by malaria (n=5); rabies (n=3); hepatitis B, Japanese encephalitis, typhoid fever, and measles (n=2 each); influenza, cholera and polio (n=1 each). Two articles assessed multiple diseases. Most studies were cost-effectiveness analyses (n=25); nine studies included cost-minimization analysis, six studies used both cost-effectiveness and cost-benefit analysis, and four studies conducted cost-benefit analysis. Travellers in most studies went from regions with very low endemicity to regions with high or very high endemicity, which was defined differently across studies. Pre-travel interventions included: passive immunization (i.e. immunoglobulin), vaccination and medications for prevention or treatment of infection. Some pre-travel interventions included screening for disease-specific antibodies prior to immunization (i.e. passive immunization or vaccination).

Estimates of clinical effectiveness

We report detailed clinical outcomes from each study (Supplementary Appendix 3). The most frequently reported outcomes were the numbers of infections, infections prevented, and deaths due to the infection, and the probability of infection.^{11,13–16,21,26,28,30,31,33,34,36,38,40,41,43–46,48,53,54} Several analyses also reported indirect effectiveness outcomes associated with missed travel or work time due to incapacitation, such as the number of travel or work days lost due to hospitalizations, travel time for clinic visits, and the number of illness days in the intervention compared with no intervention.^{15,17,21,30,31,33,36–39,41,42,44,45,47,49,50,54} Five analyses reported the threshold of disease seroprevalence at which one intervention became clinically more effective than another.^{18–20,23,24} Only three studies incorporated secondary transmission from travellers to domestic contacts.^{13,41,45}

Cost estimates

We summarized cost estimates, which were evaluated from different perspectives to account for costs borne by different stakeholders (Supplementary Appendix 4). Costs included the direct costs of testing, passive immunization or vaccination, clinical visits (e.g. travel clinic, outpatient management, hospitalizations), vaccines, medications, other treatments for infection and additional costs associated with pre-travel interventions and infections from

the perspective of individual travellers, health payers, the healthcare system and society. Analyses from the traveller's and societal perspective often accounted for indirect costs associated with the loss of productivity, lost wages for travellers or caregivers, and days of lost travel or workdays due to illness. However, most analyses did not include costs of contact tracing or outbreaks; only two studies included costs for follow-up of contacts^{22,45} and only one included costs of outbreak investigation.³⁹

Outcomes and findings

We report detailed findings of analyses, grouped by disease category: clinical outcomes, costs, variables to which analysis was sensitive, conclusions and recommendations (Supplementary Appendix 3).

Hepatitis A. Studies focused on hepatitis A included evaluations of vaccination compared with no intervention, vaccination compared to passive immunization with immunoglobulin, and screening for immunity prior to vaccination compared to universal vaccination (i.e. 'screen, then vaccinate').^{11–26,28,53} No studies were focused in the United States after 2006 when routine childhood vaccination for hepatitis A was recommended.⁵⁵

Most studies that compared hepatitis A vaccination to passive immunization with immunoglobulin found that vaccination would be cost-effective.^{11,13–18,21,53} However, one study focused on military troops found that vaccination would be cost-effective compared with passive immunization only for troops deployed frequently to the same or similar destinations.²⁶ Another study found that vaccination would not be cost-effective because incremental health gains would be small (mean, 0.000037 quality-adjusted life years [QALYs] with ICER, 2017CA\$3.4 M/QALY gained).²² A 1991 study found that costs would exceed benefits for passive immunization or vaccination due to high administration costs, which would comprise 53% of total costs for passive immunization (1991£26 per course of prophylaxis [2022US\$65.3]) and 81% for vaccination (1991£46 per course of prophylaxis [2022US\$115.5]).⁴⁴

Cost-effectiveness would depend on the prevalence of pre-existing hepatitis A immunity when comparing universal vaccination with focused vaccination for susceptible people identified through screening for pre-existing hepatitis A immunity. Screening for immunity prior to vaccination would be cost-effective compared with universal vaccination when pre-existing immunity is greater than 35% among travellers in 1991 and 1993.^{13,15} For military personnel deployed to highly endemic countries in 1995, screening prior to vaccination would be cost-effective compared with no intervention, if the pre-existing prevalence of hepatitis A is >26% as estimated from the general population of French men aged 18–26.¹⁵

Hepatitis B. Hepatitis B studies compared different hepatitis B vaccines to each other and compared universal vaccination to screening for pre-existing hepatitis B immunity prior to vaccination for the non-immune ('screen, then vaccinate').^{27,28} Two industry-funded studies demonstrated that HEPLISAV[®] and HEPLISAV-B[®] vaccines against hepatitis B would be cost-effective compared with the Engerix-B[®] vaccine (ICER, 2011US\$25000/QALY, 2020US\$11287/QALY, respectively) for travellers in 2011 and 2020 because HEPLISAV[®]

and HEPLISAV-B[®] vaccines achieved higher and earlier seroprotection against hepatitis B and required fewer doses over a shorter time compared with the Engerix-B[®] vaccine.^{27,51}

Hepatitis A/hepatitis B. In an analysis of a combined hepatitis A/B vaccine, a universal vaccination strategy would be less costly and as effective as the ‘screen, then vaccinate’ approach in 2002 and would be cost-effective for travel clinic patients aged 25 years, 45 years or 65 years in 2003 (ICERs: 2002US\$128/vaccinated 25-year person, 2002US\$144/vaccinated 45-year person, and 2002US\$177/vaccinated 65-year person given total costs/number of vaccine protections conferred).²⁸

Influenza. Only one cost-effectiveness study focused on pre-travel influenza vaccination, specifically for travellers joining cruises. This 2002 study reported cost-savings of US\$13.66 (2022US\$24) per person vaccinated, with the greatest impact for elderly passengers given their high risk for complications associated with influenza illness.²⁹ Unlike most other analyses included in this review, this study did not account for the clinical effectiveness of the intervention and did not report the results of any sensitivity analyses.

Malaria. Four studies evaluated malaria chemoprophylaxis compared to no chemoprophylaxis.^{30–33} All found that it would be cost-effective for travellers to high endemicity areas (e.g. West Africa and sub-Saharan Africa), and for travellers who engage in higher risk behaviours for malaria exposure (e.g. no bed nets, no insect repellent, prolonged stays in high-transmission areas).^{32,33} Reimbursement of chemoprophylaxis costs played a substantial role in the value of chemoprophylaxis even to highly endemic settings.^{30,31,46} If health insurance systems partially reimbursed medication costs (compared with no reimbursement), then malaria chemoprophylaxis would be higher value because of increased uptake by travellers.^{30,31,46}

Rabies. Rabies is a rare, travel-related illness but is highly lethal; several cost-effectiveness analyses have examined different strategies for pre-exposure vaccination of travellers. In a 1996 Canadian study using a decision-tree modelling approach, pre-exposure prophylaxis would not be cost-effective for all travellers but would be cost-effective in paediatric populations at high risk of exposure to rabies or leaving for a long stay (>1 year) without rapid access to medical services.³⁴ However, this study assumed that at least 90% of all people exposed to rabies would receive PEP and did not include costs of evacuation or PEP.³⁴ Two additional studies assessed the cost-effectiveness of PrEP using available data regarding the numbers of travellers who require PEP during travel. In a 1991 analysis focused on US Peace Corps volunteers dispatched to rabies-endemic countries, rabies PrEP would not be cost-effective given robust access to high-quality rabies PEP unless the cost of the three pre-exposure vaccines is US\$7/vaccine (2022US\$17.30) or less; however, pre-exposure vaccination would be cost-effective for populations with more rabies exposures.⁵² A 2020 analysis that focused on Dutch travellers evaluated the incremental costs of pre-exposure vaccination for travellers, taking into account the likelihood of requiring PEP.³⁵ This analysis found that the 2018 WHO recommendations⁵⁶ would be cost-effective compared with prior WHO recommendations, which required additional vaccine doses and greater volume of RIG; intra-dermal administration (requiring less volume of

vaccine) would offer higher value than intra-muscular administration.³⁵ The value of vaccinating travellers at higher risk of rabies exposure before departure would be greater than vaccinating all travellers, given the reduction in costs due to avoiding RIG.³⁵

Traveller's diarrhoea. One published cost-effectiveness study assessed the value of antibiotic self-treatment of travellers' diarrhoea,⁵⁰ while no study included the risks of causing antimicrobial resistance. A 1998 study supported that antimicrobial prophylaxis against travellers' diarrhoea would be cost-effective (i.e. trimethoprim-sulfamethoxazole or doxycycline) for travellers at high risk for diarrhoea, defined as 0.24 episodes of diarrhoea per person per week.⁴⁹

More recent analyses have used cost-effectiveness analysis to examine the value of licensed or hypothetical vaccination against common causes of travellers' diarrhoea. One industry-funded 2009 analysis found that Dukoral®, a vaccine active against cholera and enterotoxigenic *Escherichia coli* (ETEC)-associated travellers' diarrhoea, would be cost-saving for both leisure and business travellers, if the rate of travellers' diarrhoea among travellers is sufficiently high.^{36,37} Another analysis assessed the potential value of hypothetical multiplex vaccines against the most common etiologies of travellers' diarrhoea for a high-risk travel population (e.g. military troops travelling to high-risk regions). This 'what if?' cost-effectiveness analysis found that such a vaccine would be cost-effective over a ten-year time horizon despite the anticipated costs of research and development and clinical studies.⁴⁷ The exception was the norovirus vaccine, which would not be cost-effective because of incidence estimates and lower likelihood that affected individuals would need clinical care; therefore, a hypothetical norovirus vaccine would cost more per each duty day lost compared with other pathogen-specific vaccines, according to a 2014 analysis.³⁸

Cholera. A vaccination program for cholera in international travellers was projected to cost 28.67 million Canadian dollars in 1991 (2022US\$40.27 million) per case prevented. Due to the very high cost of vaccination and rare cases of infections among travellers, routine vaccination would not be recommended, except for travel to regions with very high transmission rates of cholera, such as Peru in 1991 when there was a 2% attack rate and 60%–100% chance of exposure.⁴⁸

Polio. A cost-benefit analysis of a temporary recommendation by the World Health Organization to vaccinate international travellers from countries experiencing serotype 1 wild polioviruses transmission during 2014–2016 demonstrated that its benefits would outweigh its costs.³⁹ Despite considerable direct and indirect costs of implementing vaccination (US\$24 million and US\$2.4 million in 2015 [2022 US\$30 million and US\$3.0 million], respectively), avoiding polio outbreaks would result in an incremental net benefit, with 8% and 44% of model iterations resulting in no new outbreaks and 1–4 outbreaks, respectively.³⁹ This was only one of three studies that considered the clinical and economic benefits of avoiding outbreaks (see also MMR).

Typhoid fever. The cost-effectiveness of vaccinating against typhoid fever prior to travel was directly proportional to the level of endemicity in the destination country. One 2004 study recommended vaccination of travellers only to countries with very high endemicity

based on incidence of typhoid fever among travellers to specific countries, as well as travellers who visit relatives or are in close contact with the local population.⁴⁰ However, this study accounted only for the cost of vaccination and not for treating the illness. A 1994 study found that pre-travel vaccination would rarely be cost-effective due to high vaccine administration costs, low incidence of travel-related illness (<10–20 cases/1 million travellers), and low case fatality rate.⁴⁴ Similarly, a 1996 study found that vaccination would not be cost-effective for military personnel who had never been deployed given the high cost of vaccine adverse effects and lost work hours.⁵⁴ Only among travellers to regions with very high endemicity (200 cases/1 million travellers) would pre-travel typhoid vaccination be cost-effective (136 Euros/case prevented (2022US\$167)).⁴⁰

MMR. In two analyses from 2019 and 2022, the cost-effectiveness of the measles-mumps-rubella (MMR) vaccination against measles at a pre-travel health encounter for travellers from the United States would vary widely depending on destination-specific risk of exposure and age group. In both analyses, MMR vaccination would provide better value for US travellers visiting destinations with higher risks of measles exposure such as Asia or Africa, especially if travellers are previously unvaccinated (compared with a history of one dose of MMR),⁴¹ infant travellers (6–12 months),⁴⁵ or returning to communities with low rates of MMR vaccination coverage after travel.^{41,45} Both analyses also captured the projected clinical benefit of reducing transmissions within the communities to which travellers return, costs of illness, and contact tracing.^{41,45}

Japanese encephalitis. A cost–benefit analysis of vaccination against Japanese encephalitis (JE) for international business travellers to endemic areas in Asia found that the benefits of vaccination would outweigh the costs, if the length of stay is 30 days or longer for travellers staying in peri-urban areas. However, vaccination would not be cost-effective for short-term travellers to urban areas or outside of the active transmission season.⁴² Another cost-effectiveness study found that the numbers-needed-to-prevent and cost-effectiveness ratios associated with preventing one case of JE illness by vaccination would vary greatly by the travellers' itinerary. In 2017, the costs per JE case averted range from US\$0.6 billion (2022US\$0.7 billion) for travellers spending ≥30 days to US\$7.6 billion (2022US\$9.1 billion) for travellers spending <30 days in endemic areas.⁴³ The value of JE vaccination is very sensitive to the incidence of Japanese encephalitis, the cost of the vaccine, and the likelihood of recurrent travel to areas with high prevalence of JE infection.⁴³

Summary and recommendations

We summarize key conclusions and recommendations for each travel-related illness in Table 2 with consideration for current travel medicine clinical practice and research.

Discussion

This scoping review identified 44 articles that assessed the value of pre-travel interventions to reduce the incidence of communicable diseases among international travellers. The small number and limited scope of these published cost-effectiveness analyses emphasize that

more investigation of pre-travel interventions is needed to improve the quality of research and clinical practice in this field. Rigorously structured cost-effectiveness analyses are essential for travel medicine because of the range of transmission risks at destinations, emerging infections, and new interventions for travel-related diseases.⁵⁷ Travel-related diseases account for an estimated US\$12 billion (2022US\$17 billion) in lost revenue due to impact on tourism,⁵⁸ with additional costs incurred from treatment and public health response.^{59,60} Cost-effectiveness analyses could help guide policy decisions regarding pre-travel interventions and reimbursement standards.

Many studies found that pre-travel interventions would be substantially more clinically effective compared to no intervention but often not cost-effective because of the low risk of infection during travel or the high costs of vaccination. Most analyses found that pre-travel vaccination for travel-associated hepatitis A and malaria chemoprophylaxis for travellers to highly endemic areas are cost-effective. However, interventions to prevent rabies, typhoid fever, cholera, and measles are rarely cost-effective due to low risk of exposure and high administration costs (e.g. nursing time for administering an injection). Pre-travel interventions could be higher value, if societal costs (e.g. visit or vaccine costs) are reduced or risks of exposure are higher. Given the rise in global incidence of measles that is three or four times higher than the prior estimate used in cost-effectiveness analyses,^{41,45,61} MMR vaccination for international travellers would be even more economically justifiable than during the era originally assessed.

All analyses reported influential parameters in the cost-effectiveness of an intervention. The value of pre-travel interventions would improve with: increased travel frequency or longer travel duration,^{11,13,14,17,21,26,32–34,36–39,42–44} greater probability of infection during travel,^{11,13,15,16,21,22,25,26,30–33,36,38,39,41–43,45–49,52} lower prevalence of pre-existing immunity among travellers,^{11–15,18–20,25,27,34,38} higher endemicity at travellers' destination,^{14–16,32,33,35,37,40–42,45–48,51,53,54} and higher secondary transmission rates from travellers after return to their home community.^{11,41} Pre-travel interventions offer better value with higher indirect costs associated with lost workdays^{11,13,14,21,26,36,38,39,49,50} and lower costs of immunization or serological testing.^{12–14,16–18,20,23,24,27,28,31–33,35,36,38,41,44,46,49,52} Immunization-specific parameters were also influential: increasing access and adherence to the intervention,^{11,15,16,23,24,27,30–34,47} higher proportion of unvaccinated travellers⁴¹ and faster uptake of immunization.^{16,47} The sensitivity of the reported findings to these key parameters may explain why substantial variability has been observed in cost-effectiveness assessments. Additionally, many published studies used clinical outcomes (e.g. cost per illness averted) that are challenging to compare with interventions for other diseases. For this reason, the Second Panel on Cost-effectiveness Analysis recommends quantifying outcomes as dollars per QALY gained to facilitate comparisons of different outcomes.¹⁰

Cost-effectiveness analyses also produce population- and setting-specific results, which account for differences in clinical characteristics, levels of endemicity at destination, risk of infection, as well as direct and indirect costs associated with pre-travel interventions, treatment, complications, and lost productivity due to incapacitation. The cost-effectiveness of an intervention is often highly dependent on the group of travellers in question (e.g.

tourists, students, military) due to differences in age, seroprevalence of immunity, and risks of exposure. Although model outcomes depend on the reliability of input estimates, such as clinical characteristics or costs associated with the intervention and treatment, performing sensitivity analyses across a range of values for these parameters allows for a systematic evaluation of the impact of this uncertainty. Additionally, cost-effectiveness analyses can be used as ‘what if?’ analyses to project the potential clinical implications and costs associated with novel interventions that are not yet available. We found one example of such an analysis in the travellers’ diarrhoea literature, which highlights how cost-effectiveness analyses can be used to examine important elements of a hypothetical vaccination to demonstrate the potential value of its further development.⁴⁸

The economic evaluations of pre-travel interventions identified in this scoping review have several strengths and some limitations. Most studies included detailed direct cost estimates. However, costs of illness were too frequently omitted, and fewer than half of the analyses accounted for the indirect costs of disease-related productivity losses, as well as the value of coverage and reimbursement of pre-travel interventions. When included, indirect costs were from the perspective of the travelling population, rather than the population to which travellers return or additional destinations that the travellers could visit, which may underestimate the impact of pre-travel interventions by focusing on the individual traveller’s risk rather than community risk, which does not account for the societal ramifications of transmissions between communities.⁶² Additionally, the value of a life saved, such as preventing rabies or malaria, was rarely explicated. Lastly, these analyses did not incorporate the individual traveller’s perspectives on risks and benefits. Most existing studies focused on population-level outcomes, which are primary focus of guidelines from international organizations like WHO and national public health agencies; however, individuals make their own decisions regarding which pre-travel interventions to pursue. Future work could quantify and weigh risk perceptions and budget constraints to provide actionable suggestions to individual travellers.

This scoping review highlights limitations of work in this field. Many studies were published more than 15 years ago and are not focused on contemporary topics in travel medicine. The 20 analyses regarding hepatitis A or hepatitis B vaccination are likely to yield different findings now given widespread childhood vaccination. One study on rabies assessed post-exposure prophylaxis with intradermal 2-dose vaccination,³⁵ which is not available for travellers in the US where no products are currently licensed for intradermal administration.⁵⁷ Studies regarding Dukoral[®] to prevent cholera have limited applicability in the US, where the vaccine is not available.⁶³ Although one study found that norovirus vaccine for US military troops would not be cost-effective,³⁸ such results could be influenced by repeated norovirus outbreaks as have been reported on cruise ships. A 1998 study found antimicrobial prophylaxis with trimethoprim-sulfamethoxazole or doxycycline for travellers at high risk for traveller’s diarrhoea would be cost-effective,⁴⁹ but increasing antimicrobial resistance and poor efficacy has been observed both for antibiotics since the 1980s, and no guidelines currently recommend either for traveller’s diarrhoea.⁶⁴ No traveller’s diarrhoea-focused models incorporate the societal benefits of reducing antimicrobial resistance. Similarly, increasing antimicrobial resistance among cases of typhoid fever could be prevented with effective vaccination but is not considered in

the 1994 cost-effectiveness study.⁶⁵ This review identified no studies that assessed cost-effectiveness of pre-travel interventions for yellow fever, although such research would be highly relevant considering the 2017 yellow fever epidemic in Brazil⁶⁶ and the absence of FDA-approved yellow fever vaccine in the US from July 2017 until April 2021.^{67–69} We were unable to make direct comparisons between studies because they used a wide variety of definitions of clinical impact and cost-effectiveness, as well as comparing the pre-travel intervention against different ‘no intervention’ scenarios. Last, we focused on travel-related infectious diseases and did not assess pretravel advice or planning for non-infectious health issues (e.g. injury, altitude illness) during travel.

In summary, we identify a substantial research gap in travel medicine. To further develop the necessary evidence base to improve both individual-level and population-level outcomes, it is essential to expand public health infrastructure to support high quality data collection regarding risks of exposure, clinical outcomes, risk perception, and costs of communicable diseases affecting international travellers.⁷⁰ Consortia have been built, including Global TravEpiNet (GTEN), which systematically collects data regarding pretravel clinical practice in the US, and GeoSentinel, which captures post-travel clinical presentations among travellers globally.^{71,72} Such programs have been leveraged to gather data on emerging infections and urgent issues arising due to international travel,^{73,74} as well as to consider important health threats that have not typically been tied to travel, such as antimicrobial resistance.⁷⁵ As such, these consortia provide an evidence base for the practice of travel medicine. Additionally, emerging technologies, such as airplane wastewater sampling and app-based symptom checkers, also have shown potential to gather detailed surveillance data in travellers and guide travellers’ decisions on pre-travel health measures.^{76–87} Studies that quantify the personal and societal costs resulting from travel-related communicable diseases will help to further understand the cost-effectiveness of different prevention or treatment strategies.^{60,88}

We propose that global collaborative networks should be maintained and expanded to leverage novel methods and to gather data on traveller characteristics and risks so that important questions related to travellers’ health can be systematically answered. Although the Advisory Committee on Immunization Practices (ACIP) develops thoughtful recommendations regarding travel-related vaccinations, the use of detailed clinical data from travellers and economic evaluations has been inconsistent and can be strengthened.^{89–92} International societies, such as the Infectious Diseases Society of America (IDSA) and the International Society of Travel Medicine (ISTM), could take the initiative to update and disseminate clinical guidelines for pretravel health care that include consideration of costs and cost-effectiveness.⁹³ By strengthening the evidence base for travel medicine, we can improve the quality and value of pretravel interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

This work was supported by US Centers for Disease Control and Prevention [U01CK000633; U01CK000175] and the Claflin Distinguished Scholars Award (EPH). The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the funders.

Data availability

No new data were generated or analysed in support of this research.

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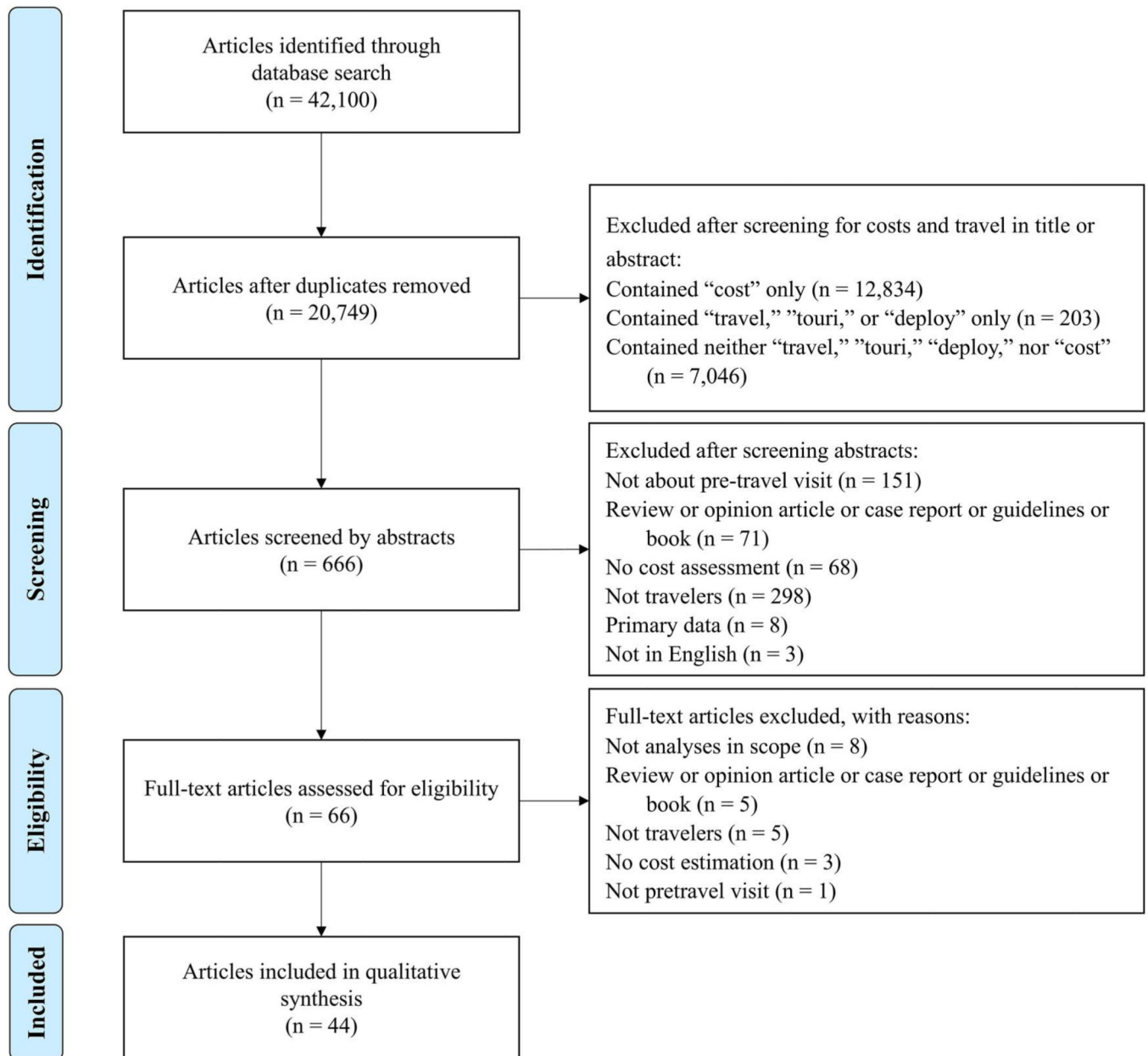


Figure 1.

PRISMA study flow diagram. The PubMed search resulted in 42 100 articles from January 1946 to January 2024. Following the removal of duplicates, 20 749 articles remained, of which 20 348 were excluded because the terms 'costs' and a travel-related term ('travel,' 'touri[st/sm],' or 'deploy') were not included in the title or abstract. The remaining 666 articles were selected for screening, of which 600 articles were excluded after abstract screening and 22 additional articles were excluded after full-text screening. Three articles were added after a search of references from the full-text articles. In total, 44 articles were selected for inclusion

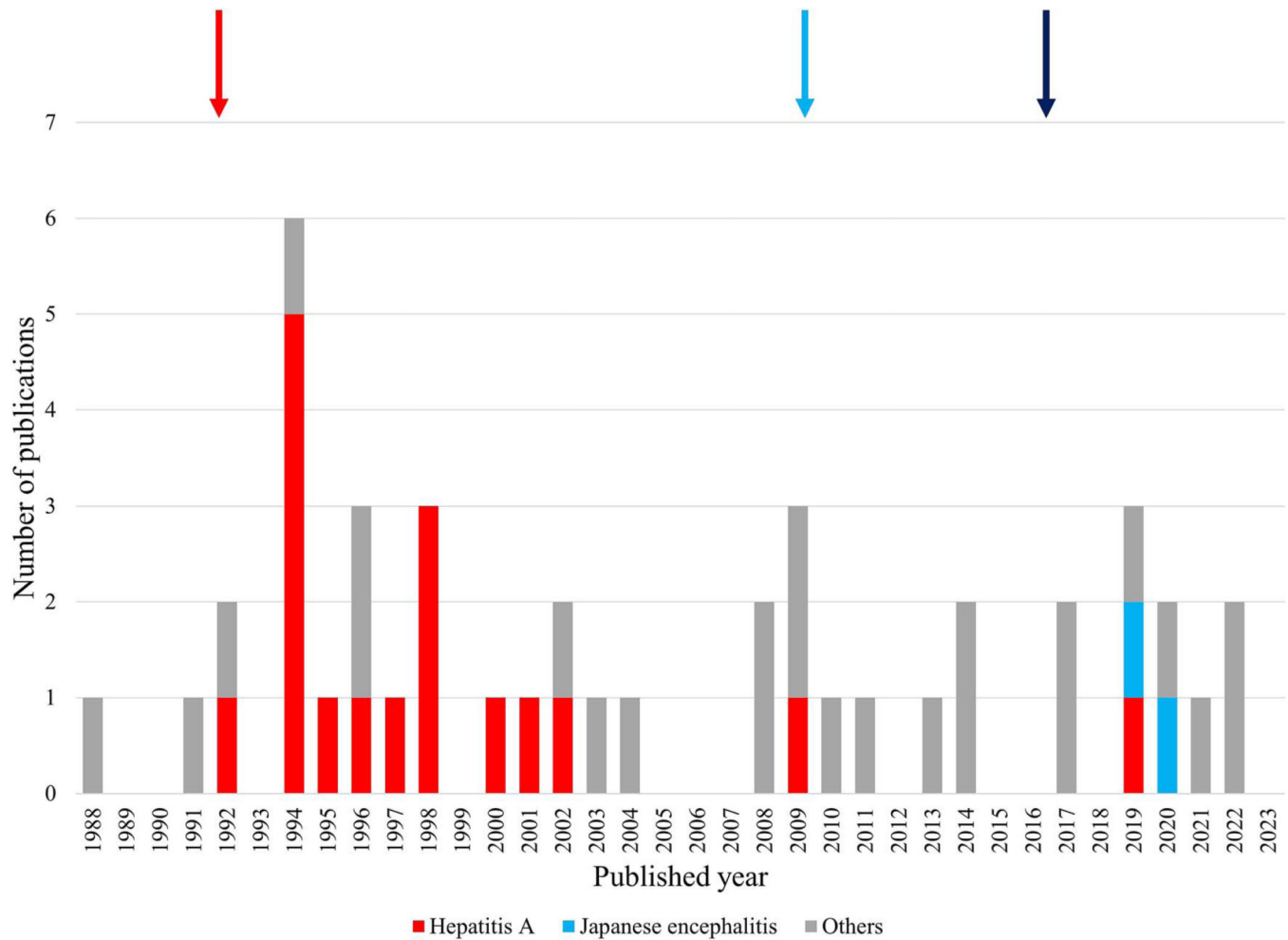


Figure 2.

Articles regarding the cost-effectiveness of pre-travel medicine selected for scoping review by year of publication, juxtaposed against the timeline of approved vaccines for hepatitis A, Japanese encephalitis, and cholera (1988–2022). The number of articles published in each year (y-axis) is shown from 1988 to 2022 (x-axis). Five travel-related vaccines were approved before 1988: influenza (1945), polio (1955), measles-mumps-rubella (1971), hepatitis B (1981). A vertical arrow shows the year in which more recent vaccines were approved (hepatitis A, red 1992; Japanese encephalitis, blue 2009; cholera, black 2016), and colour-matched bars show the number of cost-effectiveness analyses that were published after the approval of the vaccine. The remainder of published cost-effectiveness analyses that examine other pre-travel strategies to prevent communicable diseases are shown in grey

Table 1
Overview of the key characteristics of cost-effectiveness articles in travel medicine included in the scoping review

Article (1 st author, year, ^{ref} assessment method)	Population	Intervention(s)	Travellers' origin	Travellers' destination
<i>Hepatitis A</i>				
Tormans, 1992, ¹¹ cost-effectiveness	Belgian travellers (mean age 40 years; 40% naturally immune due to a previous infection)	(1) Active vaccination with hepatitis A vaccine (2) Screening for HAV antibodies and vaccinating only susceptible patients (3) Passive immunization with immunoglobulin	Belgium	Highly endemic countries
Bryan, 1994, ¹² cost-minimization	Simulated US population between 1976 and 1980, by age group	(1) Immunoglobulin without serologic testing (2) Immunoglobulin with serologic testing	United States	Highly endemic countries
Doorslaer, 1994, ¹³ cost-effectiveness	A hypothetical cohort of 100 000 travellers leaving from a country with very low, low or moderate endemicity, for short and long durations of stay, and for high and low travel frequency	(1) Active vaccination with hepatitis A vaccine (2) Active vaccination with single-dose formulation (3) Screening for HAV antibodies & vaccinate susceptibles, combined with (1) (4) Screening for HAV antibodies & vaccinate susceptibles, combined with (2) (5) Passive immunization w/immunoglobulin	Regions with range of endemicity levels: very low (Scandinavia), low (North America, Western Europe), moderate (Southern, Central, Eastern Europe)	Highly endemic countries
Tormans 1994, ¹⁴ cost-effectiveness	Belgian travellers, also applied to EU and US travellers	(1) Active vaccination (2) Screening for antibodies & vaccination of susceptibles (3) Passive immunization	Very low, low, and moderately endemic countries	Highly endemic countries
Severo, 1995, ¹⁵ cost-effectiveness	(1) Alternative military service volunteer: in developing countries (2) Tourists visiting highly endemic area (3) Hospital workers	(1) Gamma globulin prophylaxis (2) Systematic vaccination without screening (3) Systematic screening and vaccination of nonimmune persons	France	Highly endemic countries (Africa, Asia, Oceania, Americas)
Amal, 1997, ¹⁶ cost-effectiveness	Spanish travellers by age group (children and adolescents)	(1) Active vaccination (selective or nonselective) (2) Passive immunization (selective or nonselective)	Spain	Highly endemic countries
Buma, 1998, ⁵³ cost-benefit and cost-effectiveness	Dutch troops	(1) Passive immunization for all (2) Inactivated vaccine for all (3) Inactivated vaccine for susceptible individuals with screening	Netherlands	An endemic area
Fenn, 1998, ¹⁷ cost-effectiveness	Individuals who have consulted their general practitioner or otherwise sought protection 2–4 weeks prior to the departure date of a known trip to an 'at risk' area	(1) Passive immunization with immunoglobulin (2) hepatitis A vaccine	N/A	Countries 'at risk' for hepatitis A
Fishbain, 2002, ¹⁸ cost-minimization	Active-duty military service members, retirees, and dependents, and US Dept of Defence civilian employees who travel overseas on official duties	(1) Empirical vaccination of all patients (2) Serological screening of all patients plus vaccination of those seronegative	United States	N/A
Schwartz, 1998, ¹⁹ cost-minimization	Travellers (range 22–74 years) expecting to spend > = 6 months abroad who presented to travel clinic for pre-travel advice and vaccination	(1) Screening for hepatitis A IgG in pre-travel clinic prior to vaccination (2) Hepatitis A vaccination without screening	Israel	Endemic areas (not specified)

Author Manuscript	Author Manuscript	Author Manuscript	Author Manuscript	Author Manuscript
Article (1 st author, year, ^{ref} assessment method)	Population	Intervention(s)	Travellers' origin	Travellers' destination
Buckley, 1996, ²⁰ cost-minimization	Patients in a general practice travelling to destinations where immunization for hepatitis A is recommended	(1) Screening for HAV before vaccination (2) Immediate vaccination without pre-screening	United Kingdom	Endemic areas (not specified)
Jefferson, 1994, ²¹ cost-benefit and cost-effectiveness	British Army personnel and soldiers deployed to high-risk areas for a variable number of times within 5 years	(1) Active vaccination against hepatitis A (2) Passive immunization against hepatitis A	United Kingdom	Areas of high endemicity (not specified)
Ramsay, 2019, ²² cost-effectiveness	Canadian travellers to endemic countries from 2016 Ontario population	(1) Expanded public hepatitis A vaccination program for travellers to endemic countries (2) Status quo comparator: existing privately purchased access to hepatitis A vaccination for travellers who are not at high risk	Canada (Ontario province)	Endemic areas (not specified)
Costas, 2009, ²³ cost-minimization	Spanish travellers aged > 40 years travelling to international endemic areas	(1) Direct vaccination of all travellers > 40 years (2) HAV antibodies screening and vaccination of travellers without significant antibody titers	Spain	Endemic areas (not specified)
Bayas, 2001, ²⁴ cost-minimization	Spanish adult travellers of ages 18-55 years travelling to regions highly-endemic for HAV	(1) Vaccination strategy: vaccination against HAV of all persons in the target group (2) Screening strategy: HAV antibody testing and vaccination of seronegative persons	Spain	High endemicity countries in Eastern Europe, Central and South America, Asia, and Africa
Lee, 2000, ²⁵ cost-minimization	Members of Kaiser Permanente health plan (18-82 years) who were travelling to non-industrialized countries from June 1995-April 1996.	(1) Pre-vaccination screening for anti-HAV (2) Vaccination of all travellers without conducting pre-vaccination screening	United States (California only)	Non-industrialized countries (not specified)
Jefferson, 1994, ²⁶ cost-benefit and cost-effectiveness	Troops on United Nations tours in Yugoslavia, divided into subgroups of high- and low-susceptibility based on endemicity in country of origin.	Mass vaccination of military troops: (1) Active (vaccination) (2) Passive (human immunoglobulin)	Various UN countries (29)	Yugoslavia
<i>Hepatitis B</i> Kuan, 2013, ²⁷ cost-effectiveness	International travellers who are 18 years and older, travelling to countries with high HBV infection prevalence	(1) Hepatitis B vaccination using HEPLISAV vaccine (2) Hepatitis B vaccination using Engerix-B® vaccine	United States	Countries with high prevalence (not specified)
Hirst, 2021, ⁵¹ cost-effectiveness	Travellers going to hepatitis B endemic countries	(1) Hepatitis B vaccination using HEPLISAV-B vaccine (2) Hepatitis B vaccination using Engerix-B® vaccine	United States	Hepatitis B endemic countries
<i>Multiple diseases (hepatitis A and hepatitis B)</i> Jacobs, 2003, ²⁸ cost-effectiveness	College students and military recruits; 25y, 45y, and 65y travellers to hepatitis A-endemic areas	(1) Screen and defer vaccination (2) Screen and begin vaccination (3) Vaccinate without screening	United States	Endemic countries (not specified)
<i>Influenza</i> Ruben, 2002, ²⁹ cost-minimization	Crew members and travellers on cruise ships	Routine annual influenza vaccination	NY, Baltics, Tahiti, Hawaii, Sydney, Yukon	Montreal, Baltic, Hawaii, Tahiti, Alaska, New Zealand

Article (1 st author, year, ^{ref} assessment method)	Population	Intervention(s)	Travellers' origin	Travellers' destination
Article (1 st author, year, ^{ref} assessment method)	Population	Intervention(s)	Travellers' origin	Travellers' destination
<i>Malaria</i>				
Pistone, 2008, ³⁰ cost-effectiveness	French resident travellers to sub-Saharan Africa in 2005	Malaria chemoprophylaxis with (1) 0% reimbursement (2) 65% reimbursement	France	Sub-Saharan Africa
Widmer, 2010, ³¹ cost-effectiveness	Travellers medically insured in Switzerland for chemoprophylaxis	Malaria chemoprophylaxis with (1) 0% reimbursement (2) 80% reimbursement	Switzerland	West Africa
Massad, 2011, ³² cost-benefit and cost-effectiveness	United Kingdom residents travelling to 5 high and low malaria endemic regions	Malaria chemoprophylaxis using 3 different prophylaxis agents: atovaquone/proguanil, mefloquine, doxycycline	United Kingdom	Brazil, India, Nigeria, Thailand, Indonesia, Ghana, Sierra Leone
Adachi, 2014, ³³ cost-benefit	US travellers to West Africa by travel purpose - visiting friends and relatives, business, leisure	(1) No intervention (2) Health consultation on insect bite prevention and malaria chemoprophylaxis	United States	West Africa
Fiorina, 2022, ⁴⁶ cost-effectiveness	Travellers heading to malaria endemic regions in sub- African countries	Malaria chemoprophylaxis reimbursement scenario, compared to 0% reimbursement: (1) 65% reimbursement by National Health Insurance (NHI) not affecting the current chemoprophylaxis using population (2) 65% reimbursement increasing the use of atovaquone/proguanil with higher compliance rates	France	Sub-Saharan Africa, West and Central Africa
<i>Rabies</i>				
LeGuerrier, 1996, ³⁴ cost-effectiveness	Travellers to rabies-endemic areas (1 million in each of the 2 subgroups)	(1) Post-exposure prophylaxis (2) Pre-exposure vaccination + post-exposure prophylaxis	Canada	Rabies-endemic regions (not specified)
Bernard, 1991, ⁵² cost-minimization	US Peace Corps volunteers at risk for rabies serving in endemic countries	(1) Post-exposure prophylaxis (2) Pre-exposure vaccination + post-exposure prophylaxis	United States	Africa, Asia Pacific, Latin America ¹
Suijkerbuijk, 2020, ³⁵ cost-effectiveness	Dutch travellers potentially exposed to rabies abroad, following an animal-associated injury	Pre-exposure vaccination + post-exposure prophylaxis • Past WHO recommendations vs 2018 WHO • Intramuscular administration vs intradermal administration • More travellers than currently vaccinated	Netherlands	Rabies-endemic countries (not specified)
<i>Travellers' diarrhoea (TD)</i>				
Reves, 1988, ⁴⁹ cost-effectiveness	Placebo-treated or untreated Peace Corps volunteers	(1) Treatment with TMP-SMX (2) Daily prophylaxis with doxycycline or TMP-SMX	United States	Kenya, Morocco, Honduras, Thailand
Riddle, 2008, ⁴⁷ cost-effectiveness	Cohort of 147 000 troops deployed for 3.5 months	(1) Standard of care (antimicrobial treatment) (2) Multiplex and pathogen-specific vaccines against TTD	United States	Highly endemic
Lundkvist, 2009, ³⁶ cost-benefit	Leisure and business travellers	(1) No vaccination (2) Oral cholera vaccine	Canada	Endemic areas

Article (1 st author, year, ^{ref} assessment method)	Population	Intervention(s)	Travellers' origin	Travellers' destination
López-Gigoso, 2009, ³⁷ cost-benefit and cost-effectiveness	Travellers attending 2 International Vaccination Centers in Spain (3.3% business, 96.7% tourists)	(1) No vaccination (2) Oral whole-cell/recombinant B-subunit cholera vaccine (WC/rBS) - Dukoral [®]	Spain	High-endemicity zones in Africa, Americas, SE Asia
Tallant, 2014, ³⁸ cost-effectiveness	United States military troops in forward deployed settings	(1) Vaccination for norovirus (2) Current management (i.e. no treatment)	United States	N/A
Schrader, 2017, ⁵⁰ cost-effectiveness	50 000 military deployment service members	(1) Increased probability and earlier seeking of healthcare by deployed service members (2) Increased probability of military healthcare providers prescribing a single-dose antibiotic with loperamide (3) Combination of (1) and (2)	United States	Areas with monthly incidence of TD at 28.9%
<i>Cholera</i>				
MacPherson, 1992, ⁴⁸ cost-effectiveness	North American travellers to endemic areas	(1) No cholera vaccination (2) Cholera vaccination	Canada	Endemic areas (inputs partially based on Peru)
<i>Polio</i>				
Duintjer Tebbens, 2017, ³⁹ cost-benefit	International travellers from countries with transmission of serotype 1 wild polioviruses (WPV1s)	(1) No intervention (2) World Health Organization's temporary recommendation to vaccinate travellers	Afghanistan, Cameroon, Pakistan	Other countries (not specified)
<i>Typhoid fever</i>				
Warren, 1996, ⁵⁴ cost-effectiveness	(1) military personnel never deployed (2) military personnel already deployed to an endemic area	(1) No intervention (2) Typhoid Vaccine USP (a 2-dose inactivated vaccine) (3) Vivotif (a 4-dose oral live vaccine) (4) Typhim-Vi (a single-dose subunit vaccine)	United States	An endemic area
<i>Typhoid fever</i>				
Papadimitropoulos, 2004, ⁴⁰ cost-effectiveness	Travellers from the US to developing countries in 1974–1994	(1) Oral live-attenuated vaccine (Ty21a) (2) Capsular polysaccharide parenteral Vi	United States	Moderately, highly, and very highly endemic countries
<i>Measles</i>				
Hyle, 2019, ⁴¹ cost-effectiveness	US resident international travellers born after 1956	(1) MMR vaccination at a pre-travel health encounter (2) No vaccination	United States	Hotspots: Philippines, India, Pakistan, Poland
Bangs, 2022, ⁴⁵ cost-effectiveness	US paediatric travellers aged 6 months to < 6 years	(1) Pre-travel health encounter (2) Pre-travel health encounter where MMR vaccination is offered	United States	Each of the continents
<i>Japanese encephalitis (JE)</i>				
Rogers, 2019, ⁴² cost-benefit	International business/occupational travellers to Asia	(1) No vaccination (2) vaccination	United States	Endemic areas in Asia
Carias, 2020, ⁴³ cost-effectiveness	US travellers travelling to locations with varying JE risk: 1) travellers spending > = 1 month in JE-endemic areas; 2) < 1 month-travellers spending > = 20% time on outdoor activities in rural areas; 3) all remaining travellers	(1) No vaccination (2) vaccination with 2y booster	United States	Endemic countries (not specified)

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Article (1 st author, year, ^{ref} assessment method)	Population	Intervention(s)	Travellers' origin	Travellers' destination
<i>Multiple diseases (malaria, hepatitis A, typhoid fever)</i> Behrens, 1994, ⁴⁴ cost–benefit and cost-effectiveness	United Kingdom residents visiting endemic areas in 1991	Pre-travel prophylaxis (1) 3 options for typhoid fever: Typhoid Ty 21a vaccine, Typhoid Vi vaccine, Whole cell killed monovalent vaccine (2) 2 options for hepatitis A: immunoglobulin or vaccine (3) 2 options for malaria: Chloroquine+ proguanil or Mefloquine	United Kingdom	Endemic countries (not specified)

Table 2

Conclusions and recommendations from economic evaluation studies focused on pretravel health interventions for communicable diseases

Disease	Conclusions and recommendations	References
Hepatitis A	-Vaccination is cost-effective compared with no prevention. -Given widespread childhood vaccination since 2006, screening for hepatitis A antibody prevalence may be more cost-effective than universal vaccination in the absence of documented vaccination.	11–26,53
Hepatitis B	-Limited data are available regarding the cost-effectiveness of vaccination among travellers; both studies are industry-sponsored comparisons of types of hepatitis B vaccination. -Given broader recommendations for hepatitis B vaccination in the general population, pretravel evaluations offer an opportunity for improving vaccination among the eligible.	27,51
Hepatitis A & Hepatitis B	-Given widespread childhood vaccination, screening for antibodies may be cost-effective rather than universal vaccination in the absence of documented vaccination. -Given broader recommendations for hepatitis A and hepatitis B vaccination in the general population, pretravel appointments offer an opportunity for improving uptake among the eligible.	28
Influenza	-Seasonal influenza vaccination is recommended as a part of routine immunization, but uptake is low and travellers are likely at increased risk for illness given different seasonality in hemispheres. -A limited modelling analysis focused on cruise travel found that vaccination of elderly travellers would be cost-effective; further study is warranted given the seasonal frequency of influenza and low uptake of vaccination despite efficacy.	29
Malaria	-Chemoprophylaxis is cost-effective for travellers to highly endemic regions (e.g. West Africa) and could be cost-effective for longer visits to other endemic regions. -Reducing costs of malaria chemoprophylaxis to the traveller (e.g. reimbursement) could improve uptake and further improve its value.	30–33,46
Rabies	-Pre-exposure prophylaxis would be cost-effective only for children at high risk of exposure, for > 1y stay, or without rapid access to healthcare. -Communicating risks of infection, bite avoidance, and post-bite prophylaxis is integral for travellers, especially to high-risk regions.	34,35,52
Travellers' diarrhoea	-The prophylaxis strategies assessed in cost-effectiveness analyses are no longer applicable given rates of antibiotic resistance. -No cost-effectiveness analyses have been published that account for current incidence of bacterial etiologies of travellers' diarrhoea, antibiotic resistance patterns, risks of developing antibiotic resistance, and traveller comorbidities. -Modelling analyses have suggested the benefit of a vaccine to prevent common causes of travellers' diarrhoea.	36–38,47,49,50
Cholera	-Combining food and water precautions and handwashing is highly recommended; vaccination would be cost-effective only for travellers to high transmission regions in one industry-sponsored study.	48
Polio	-Benefits of vaccinating travellers outweigh costs when travellers go to areas of active virus circulation. -Easily accessed estimates of polio risk globally are important to identify when polio vaccine is recommended for travellers.	39
Typhoid fever	-Vaccination is cost-effective for travellers to highly endemic areas, visiting friends and relatives, or in close contact with local communities. -Improved estimates of typhoid fever incidence from different settings would be helpful to refine recommendations.	40,54
Measles	-MMR vaccination for eligible international travellers would be effective and cost-effective for international travellers to areas with high-risk exposure and people previously unvaccinated or partially vaccinated. -Given rising measles incidence globally, MMR vaccination could be cost-effective regardless of the destination.	41,45
Japanese encephalitis	-Vaccination would be economically beneficial for people frequently travelling to endemic areas or staying >=30 days during 1 or more transmission seasons, as well as for business travellers travelling to endemic areas for 2 weeks or longer during transmission season. -Combined with vaccination, travellers should avoid mosquito bites using repellent and bed nets.	42,43

Note: One study addressed multiple diseases, of which the findings are incorporated into each disease's findings.⁴⁴