

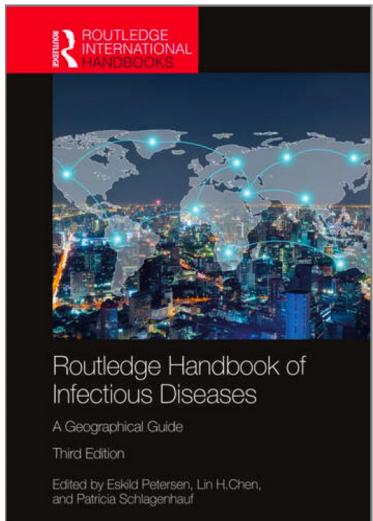


The Year in Travel Medicine: Papers that Influence Practice

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Associate Professor of Medicine, Harvard Medical School
Past President, International Society of Travel Medicine
NECTM9, Copenhagen, Denmark, May 24, 2024



Disclosures



- Collaborations/honoraria/advisor fees:
 Shoreland, Valneva, Takeda, Merck, Bavarian
 Nordic
- Data Safety Monitoring Boards: Valneva
- Royalties: "Infectious Diseases: A Geographic Guide"

Selection

- TOC 12 months... JTM, TMAID, NEJM, Lancet, CID, JID...
- PubMed search [international travelers]
 [travel-related] [malaria] [dengue] combo
- >1200 titles → 120 higher interest
- Categories overlap: pre-travel, vaccines, yellow fever, malaria, TD, during-travel, post-travel, AMR, emerging infections...
- Impact on travel medicine practice





Ngieam JN et al. J Travel Med. 2024 Jan 28;31(1):taad124

INTERNATIONAL SOCIETY OF TRAVEL MEDICINE

Journal of Travel Medicine, 2024, 1–3 https://doi.org/10.1093/jtm/taad124

Research Letter

Research Letter

Artificial intelligence models for pre-travel consultation and advice: yea or nay?

Jinghao Nicholas Ngiam, MBBS^{1,*}, Matthew Chung Yi Koh, MD¹, Priscillia Lye, MBBS¹, Tze Sian Liong, MBBS², Brenda Mae Alferez Salada, MD^{1,3}, Paul Anantharajah Tambyah, MBBS^{1,3,4} and Jolene Ee Ling Oon, MBBCh BaO^{1,3}

Background

- ChatGPT is AI chatbot that creates dialogue with user
- What is AI role in Travel Medicine education and aid pre-travel prep?

Methods

- Instructed ChatGPT to give pre-travel advice, then provided application with a series of commonly-asked pretravel queries (e.g. food/water safety, sexual health, traveller's diarrhoea), vaccinations and malaria prophylaxis
- Compared accuracy and appropriateness of responses vs
 CDC Yellow Book 2024 and Shoreland Travax.

Results

- ChatGPT answers were accurate, but generic, not contextualized.
- Did not recognize: high quinolone resistance, Kilimanjaro as high-altitude risk, meningococcal required for Hajj pilgrims, account for PMH/ comorbidities/ prior immunization/ specific geographic area of travel.

Conclusions

- Al chatbots for pretravel advice may be vital and complementary to physical consultation, but lacks contextualizing advice
- Human travel medicine provider still can fill the gap for the individualized advice

Strengths and weaknesses of ChatGPT for pre-travel consultation and advice

Ngiem JN et al. J Travel Med. 2024 Jan 28;31(1):taad124

Questions	Strengths	Limitations
General travel advice Should I seek a pre-travel clinic consultation prior to travelling? How can I avoid falling sick overseas? What precautions do I have to take for food and water safety overseas? Are there recommended additional precautions with regards to sexual health overseas? What can I take for traveller's diarrhoea? How can I take precautions against altitude sickness?	Information provided is generally concise and accurate, given in point-form for ease of reading Appropriately and consistently recommends consultation with healthcare provider or travel clinic in addition to the specific advice given Gives accurate advice on food and water safety, safe sex, traveller's diarrhoea and altitude sickness	Generic advice is not contextualized to the specific details of the travel itinerary Also does not take into account the specific details of the traveller's background and medical comorbidities Gives both ciprofloxacin and azithromycin as options for traveller's diarrhoea which may not be appropriate in all regions of travel
Vaccinations When should I get my pre-travel vaccines? Can I take my vaccinations if I am on high-dose steroids? Can I take the yellow fever vaccine if I am on steroids? What precautions do I need for travel to Mecca for the Haj? Is the meningococcal vaccine required for Haj pilgrimage? What vaccines are required for travel to Bogota, Columbia? What are some risks associated with vaccinations? What are some risks associated with Yellow	Appropriately and consistently advises further discussion with a healthcare provider or travel clinic Recommends the appropriate timing for vaccinations and also explains the potential utility in specific settings for last-minute vaccinations Appropriately identifies and explains the need for Yellow Fever vaccination in at-risk areas.	Does not mention meningococcal vaccine specifically for Haj, unless prompted Explanation for the vaccine-associated viscerotropic and neurotropic disease as part of the Yellow Fever vaccination is not clear as to the nature of the complication, and does not weigh it against the risk of acquiring Yellow Fever. Also does not mention COVID-19 precautions unless prompted, with information up-to-date only up to September 2021.
Fever vaccination? Do I require COVID-19 vaccination for travel? Malaria prevention prophylaxis How can I avoid mosquitoes? Do I need malaria prophylaxis for travel to Nairobi, Kenya? What prophylaxis for malaria is recommended for travel to Abidjan? What are the options I can use for malaria prophylaxis?	Gives appropriate advice for vector avoidance. Appropriately recognises the need for malaria prophylaxis in Kenya, if in line with the nature of the travel Gives all the appropriate options for malaria prophylaxis, as well as how they are to be taken, and common side effects	Does not take into account the individual's potential co-morbidities in relation to options malaria chemoprophylaxis Did not consider geographic considerations and rates of resistance in the choice of malaria prophylaxis Also does not compare the cost of each option

Steffen RS et al. J Travel Med. 2023 Nov 18; 30(7):taad085





https://doi.org/10.1093/jtm/taad085

Tetanus

Review

Travel vaccines—priorities determined by incidence and impact

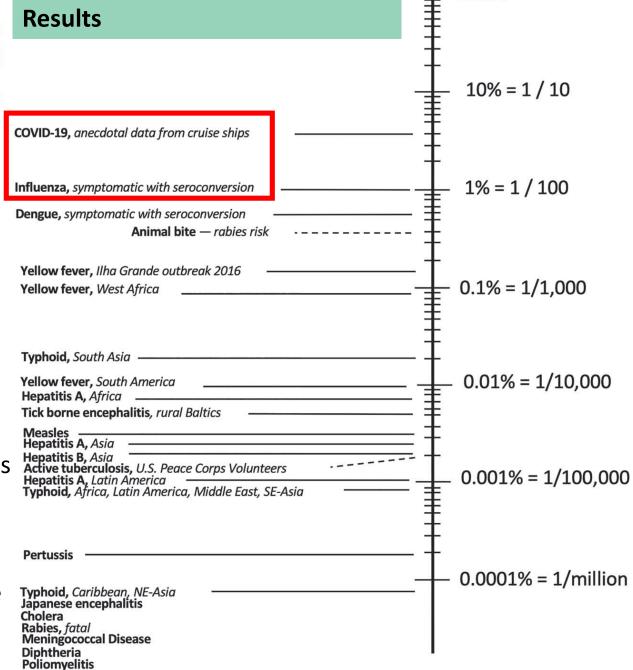
Robert Steffen, MD^{1,2,*}, Lin H Chen, MD^{3,4} and Peter A Leggat, MD, PhD, DrPH^{5,6}

Background

Infectious disease epidemiology shifts over time, need regular reassessment of vaccine in their application to travelers

Methods

- Literature search on epidemiology of travel-related VPD, synthesized data with focus on symptomatic cases and impact of respective infection among travellers, considering hospitalization rate, disease sequela and case fatality rate.
- Estimated monthly incidence rate among non-immune exposed travelers: best estimate for non-immunes



100%

Steffen RS et al. J Travel Med. 2023 Nov 18; 30(7):taad085





Journal of Travel Medicine, 2023, 1–1 https://doi.org/10.1093/jbn/taad08 Revier

Review

Travel vaccines—priorities determined by incidence and impact

Robert Steffen, MD1,2,*, Lin H Chen, MD3,4 and Peter A Leggat, MD, PhD, DrPH5,6

Results

- COVID-19 emerged as top travel-related risk
- Influenza remains high ranking: 1%/month
- Dengue: 0.5-0.8%/month in non-immune travelers
 - Hospitalization 10-22%
- YF rose due to recent outbreaks especially Brazil:
 >0.1%/month
- Some decline in foodborne illnesses
- Hepatitis A: still substantial 0.001-0.01%/month in developing regions
- Typhoid still high in South Asia: >0.01%/month

Conclusions

- Updated monthly incidence and impact of VPDs provide a tool to prioritize strategies
- Important to continue assessing with shifts in risk of travel-related health issues and new vaccines with travel indications



Schneider M et al. Lancet. 2023 Jun 24;401(10394):2138-2147.

Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial

Martina Schneider, Marivic Narciso-Abraham, Sandra Hadl, Robert McMahon, Sebastian Toepfer, Ulrike Fuchs, Romana Hochreiter,
Annegret Bitzer, Karin Kosulin, Julian Larcher-Senn, Robert Mader, Katrin Dubischar, Oliver Zoihsl, Juan-Carlos Jaramillo, Susanne Eder-Lingelbach,
Vera Buerger, Nina Wressnigg

Background

- VLA1553 live-attenuated: La Reunion strain of ECSA genotype with a 61 amino acid deletion in nsp-3
- Phase 3: safety & immunogenicity up to 180 days

Methods

- Double-blind, multi-ctr, randomized, healthy ≥18 years
- Primary endpoint: proportion of baseline negative participants that have a seroprotective CHIKV μPRNT50 titre ≥150 @28 days (50% plaque reduction in a micro plaque reduction neutralisation test)
- Safety: all subjects who received vaccination
- Immunogenicity: subset from 12 pre-selected sites

Results

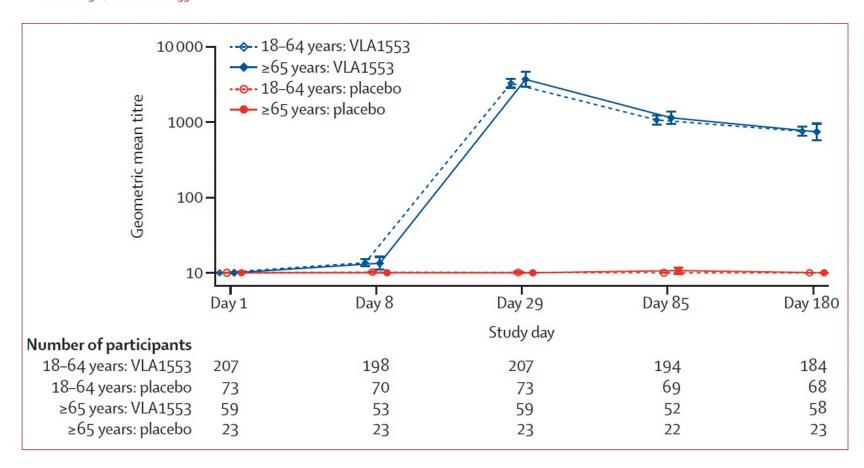
- Sept 17, 2020 and April 10, 2021: 4128 enrolled and randomised (3093 to VLA1553; 1035 to placebo); immunogenicity analysis N= 362
- VLA1553 induced seroprotective chikungunya virus neutralising antibody levels in 98.9%
 - 98.6% 18-64 years; 100% ≥65 years
- Day 180: 96.3% seroprotection
- Serious AEs in 1.5% of 3082 in VLA1553 arm vs
 0.8% of 1033 in placebo arm
- 2 related SAEs: 1 mild myalgia, 1 SIADH; recovered

Conclusions

- Live-attenuated VLA1553 led to strong immune response and generation of seroprotective titres
- 1 dose promising especially in outbreak response

Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial

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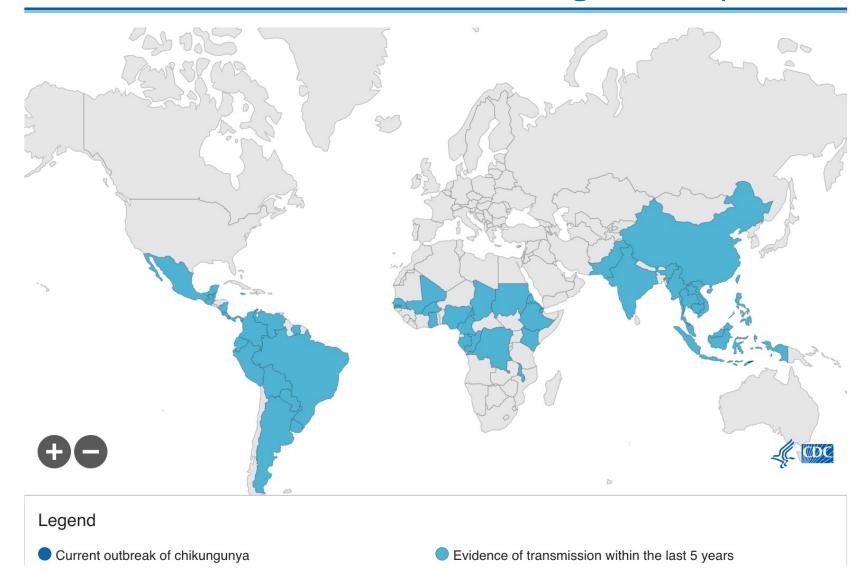


Draft recommendations

- Chikungunya vaccine is <u>recommended</u> for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak
- In addition, chikungunya vaccine <u>may be considered</u> for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years
 - Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure* to mosquitoes, OR
 - Persons staying for a cumulative period of 6 months or more

^{*}Moderate exposure could include travelers who might have at least 2 weeks (cumulative) of exposure to mosquitoes in indoor and/or outdoor settings

Countries with outbreaks or evidence of chikungunya virus transmission to humans during last 5 years



2024, **99**, 203–224



Weekly epidemiological record Relevé épidémiologique hebdomadaire

3 MAY 2024, 99th YEAR / 3 MAI 2024, 99e ANNÉE

No 18, 2024, 99, 203–224

http://www.who.int/wer

Contents

WHO position paper on dengue vaccines – May 2024

Note de synthèse: position de l'OMS sur les vaccins contre la dengue – mai 2024

203 WHO position paper on dengue vaccines – May 2024

- TAK-003: tetravalent, live-attenuated with DENV2 (TDV-2) providing backbone
- Schedule: Day 0, 3 months
- Dengue vaccination is part of integrated strategy to control dengue, along with vector control, proper case management, community education, and community engagement
- Countries in areas with high transmission intensity: introduce TAK-003 into routine immunization programs
 - Target age: 6-16 years in high transmission intensity areas
- Travellers to endemic countries: h/o previous dengue infection, frequent travellers, long-term travellers, migrants, expats
 - Age range for travellers: 6-60 years

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 1, 2024

VOL. 390 NO. 5

Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults

E.G. Kallás, M.A.T. Cintra, J.A. Moreira, E.G. Patiño, P.E. Braga, J.C.V. Tenório, V. Infante, R. Palacios, M.V.G. de Lacerda, D.B. Pereira, A.J. da Fonseca, R.Q. Gurgel, I.C.-B. Coelho, C.J.F. Fontes, E.T.A. Marques, G.A.S. Romero, M.M. Teixeira, A.M. Siqueira, A.M.P. Barral, V.S. Boaventura, F. Ramos, E. Elias Júnior, J. Cassio de Moraes, D.T. Covas, J. Kalil, A.R. Precioso, S.S. Whitehead, A. Esteves-Jaramillo, T. Shekar, J.-J. Lee, J. Macey, S.G. Kelner, B.-A.G. Coller, F.C. Boulos, and M.L. Nogueira

Background

Butantan-DV is an investigational, single-dose, live, attenuated, tetravalent vaccine against dengue

Methods

- Ongoing phase 3, double-blind trial in Brazil, randomized to Butantan-DV or placebo, stratified by:
 - 2-6 years
 - 7-17 years
 - 18-59 years
- 5 years follow-up planned

Results

Butantan-Dengue Vaccine N=10,259 Placebo N=5976





- 2-year VE= 79.6% against VCD, 90% against hospitalization
 - 73.6% in baseline seronegative vs VCD
 - 89.2% in those with past dengue

Age 2-6 y: 80.1%

7-17 y: 77.8%

18-59y: 90%

• VE DENV-1: 89.5%; DENV-2: 69.6%

DENV-3 and DENV-4 not detected

Solicited AE <21 days: vaccine 58.3%; placebo 45.6%

Conclusions

Single dose of Butantan-DV prevented symptomatic DENV-1 and DENV-2, regardless of baseline serostatus, through 2 years

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

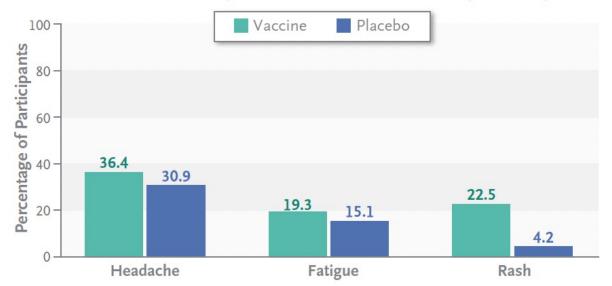
FEBRUARY 1, 2024

VOL. 390 NO. 5

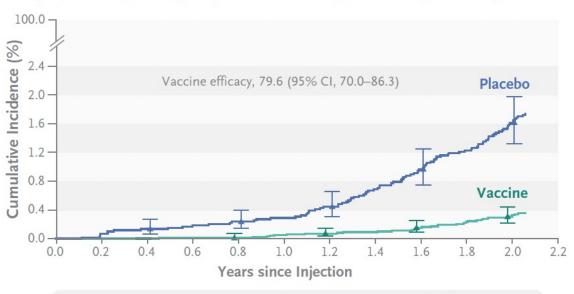
Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults

E.G. Kallás, M.A.T. Cintra, J.A. Moreira, E.G. Patiño, P.E. Braga, J.C.V. Tenório, V. Infante, R. Palacios, M.V.G. de Lacerda, D.B. Pereira, A.J. da Fonseca, R.Q. Gurgel, I.C.-B. Coelho, C.J.F. Fontes, E.T.A. Marques, G.A.S. Romero, M.M. Teixeira, A.M. Siqueira, A.M.P. Barral, V.S. Boaventura, F. Ramos, E. Elias Júnior, J. Cassio de Moraes, D.T. Covas, J. Kalil, A.R. Precioso, S.S. Whitehead, A. Esteves-Jaramillo, T. Shekar, J.-J. Lee, J. Macey, S.G. Kelner, B.-A.G. Coller, F.C. Boulos, and M.L. Nogueira

Most Common Solicited Systemic Adverse Events ≤21 Days after Injection



Symptomatic, Virologically Confirmed Dengue >28 Days after Injection



Vaccine
Estimated Incidence 0.17/100 person-yr at risk (95% CI, 0.12–0.24)

Placebo 0.84/100 person-yr at risk (95% CI, 0.68–1.02) Overduin LA et al. Lancet Infect Dis 2023 Oct 3:S1473-3099(23)00452-8.

Boostability after single-visit pre-exposure prophylaxis with

Boostability after single-visit pre-exposure prophylaxis with rabies vaccine: a randomised controlled non-inferiority trial

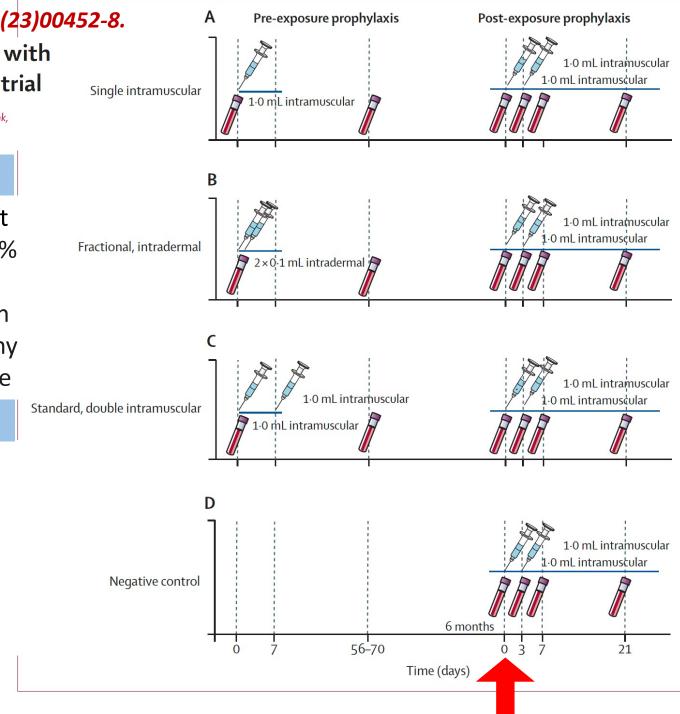
Lisanne A Overduin*, Jan Pieter R Koopman*, Corine Prins, Petra H Verbeek-Menken, Cornelis A De Pijper, Phaedra L Eblé, Fiona Heerink, Perry J J van Genderen, Martin P Grobusch, Leo G Visser

Background

- 59,000 human deaths/year worldwide, highest incidence in Asia & Africa (60%/36%), dogs 99%
- Travelers: animal bites/scratches reported frequently, estimated 1 in 300 travelers/month
- HRIG is costly and is scarce/unavailable in many countries, often requires repatriation after bite

Methods

- Block-randomised (2:2:2:1) controlled, multicentre non-inferiority trial
- Adult travellers (aged 18–50 years and >50 years), 3 Dutch travel clinics
- Primary outcome boostability: induction of rapid, anamnestic antibody response after simulated PEP, measured as increase in geometric mean RVNA from day 0 to 7



Results RVNA concentrations and boostability

Results Geometric mean RVNA

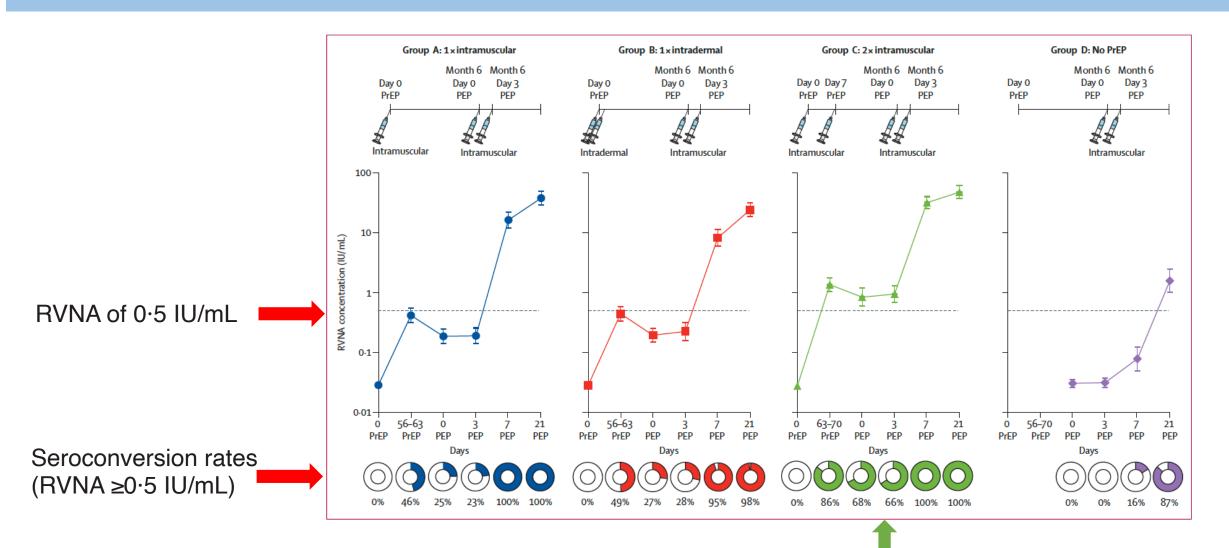
- N=214, 59% F, 15% age >50 years
- 2 months after PrEP:
 - 1-visit IM 0.42
 - 1-visit ID 0.45
 - 2-visit IM 1.38
- 6 months after PrEP similar trend
- After PEP RVNA rose rapidly in all PrEP participants, Day 7:
 - 1-visit IM 16.54
 - 1-visit ID 8.23
 - 2-visit IM 32.61

Primary outcome = boostability between PEP Day 0 and 7

- Anamnestic antibody response of 1visit IM rabies PrEP was non-inferior compared to 2-visit IM schedule
- 1-visit ID PrEP did not meet noninferiority limit for boostability

Results

Kinetics of geometric mean RVNA concentrations in participants aged 18-50 years



Conclusions

- Reduced-dose PrEP is cost-efficient, time-efficient
- Boostability data add support to 2-dose IM PrEP (as recommended by WHO, ACIP)
- For travelers, reduced-dose facilitates rabies PrEP (less time constraint, cost)
- Application is greatly beneficial to rabies endemic countries and travelers
- Limitations:
 - Excluded immunocompromised and few older persons
 - Long-term boostability at >6 months after PrEP?
 - What interval is needed for developing immune memory between 1-visit IM and potential exposure?
 - Several participants had unexplained drop of RVNA between PEP Day 0 to 7?

Hills SI et al. MMWR Recomm Rep. 2023 Nov 10;72(5):1-29.

Tick-Borne Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2023

Susan L. Hills, MBBS¹; Katherine A. Poehling, MD²; Wilbur H. Chen, MD³; J. Erin Staples, MD, PhD¹

¹Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC, Fort Collins, Colorado; ²Wake Forest School of Medicine, Winston-Salem, North Carolina; ³University of Maryland School of Medicine, Baltimore, Maryland

Background

- TBEV is focally endemic in areas in Europe through northern and eastern Asia
- Transmission: Ixodes, ingestion, breastmilk, transfusion, solid organ transplant, slaughtering viremic animals
- Clinical manifestation: subclinical to acute neurologic disease needing hospitalization, permanent neurologic or cognitive sequelae, and death
- Vaccine available in Europe since 2001
- FDA licensed (2021) TBE inactivated whole cell vaccine based on European subtype

Methods

 ACIP Work Group reviewed extensive data and evidence on TBE infection, prevention, and vaccine to develop recommendations

Results

- TBE is rarely reported in US travelers:
 - 12 civilians cases confirmed 1979-2021
 - 12 military/dependents 2012-2021
- Onset April November
- Vaccine efficacy after ≥3 doses of vaccine: 91%–
 99%
- 2-dose seropositivity rates among healthy adults at 3–4 weeks: 83%-100%
- 1-dose seropositivity rate at 12 days: 52% age 16-49y, 27% 50-79y



Tick-Borne Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2023

Susan L. Hills, MBBS¹; Katherine A. Poehling, MD²; Wilbur H. Chen, MD³; J. Erin Staples, MD, PhD¹

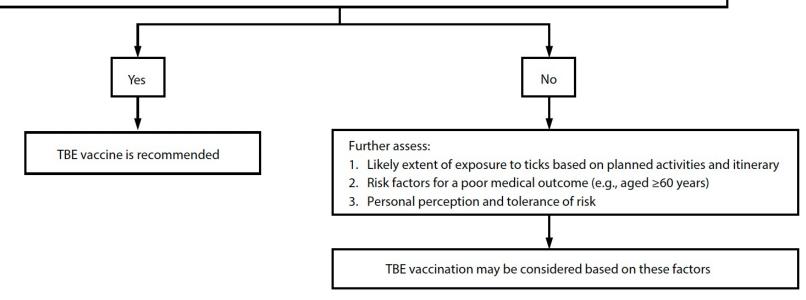
¹Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC, Fort Collins, Colorado; ²Wake Forest School of Medicine, Winston-Salem, North Carolina; ³University of Maryland School of Medicine, Baltimore, Maryland

Health care provider should assess a traveler's risk for TBE virus infection based on their planned activities and itinerary:

- 1. All travelers to countries where TBE is endemic with risk for tick exposure should take precautions to avoid tick bites. Travelers also should avoid the consumption of unpasteurized dairy products.
- 2. For certain travelers who are at increased risk for TBE, TBE vaccine might be indicated.

Is the person moving or traveling to an area where TBE is endemic and likely to have extensive exposure to ticks based on planned outdoor activities and itinerary?

Extensive exposure can be considered based on the duration of travel and frequency of exposure and might include shorter-term (e.g., <1 month) travelers with daily or frequent exposure or longer-term travelers with regular (e.g., a few times a month) exposure to environments that might harbor infected ticks.



Conclusions

Primary Series

- 1–15 years: 3 doses (0.25 mL)
 IM Day 0, 1–3 months, dose 3
 @5–12 months later.
- ≥16 years: 3 doses (0.5 mL) IM
 Day 0, Day 14-3 months, dose 3
 @5–12 months later.

Booster

≥3 years after completion of primary series

Schnyder JL et al. Lancet Glob Health 2024 Mar;12(3):e445-e456

Long-term immunity following yellow fever vaccination: a systematic review and meta-analysis



Jenny L Schnyder, Hanna K de Jong, Bache E Bache, Frieder Schaumburg, Martin P Grobusch

open access

Summary

Background Long-term immunity following yellow fever vaccination remains controversial. We aimed to summarise the literature regarding the long-term protection (≥10 years) conveyed by a single dose of yellow fever vaccination.

Lancet Glob Health 2024 12: e445–56

Background

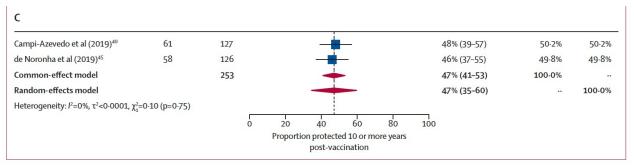
- Duration of YF vaccine protection remains controversial
- Authors summarised studies on long-term protection (≥10 years) after a single dose YF vaccine

Methods

- Searched 11 databases through Aug 24, 2023
- Included cohort and cross-sectional studies reporting immunogenicity in persons that received a single dose of YF vaccine ≥10 years earlier

Results

- Systematic review: 39 articles eligible, N=2895
- Meta-analysis: 20 studies
- Pooled seroprotection:
 - Adult: travelers/nonendemic 94% endemic/Brazil 76%
 - Children 9-23 months: 47%



Persons living with HIV: 61%

D	Number of seroprotcted vaccinees	Total number of vaccinees		Seroprotection rate, % (95% CI)	Weight (common)	Weight (random)
Avelino-Silva et al (2016) ³⁵	5	10	-	50% (19–81)	9.1%	15.6%
Veit et al (2018) ³³	47	63	1	75% (62-85)	54.7%	38.9%
Veit et al (2009)34	5	10	<u> </u>	50% (19-81)	9.1%	15.6%
Martin et al (2022) ⁶²	16	31		52% (33-70)	27.2%	29.9%
Common-effect model		114		65% (55-74)	100.0%	
Random-effects model				61% (38-82)		100.0%
Heterogeneity: I ² =56%, τ ² =0-0	0094, $\chi_3^2 = 6.83$ (p=0.078)	0 20 Proportio	40 60 80 In protected 10 or more years post-vaccination	100		

Α	Number of seroprote vaccinees	cted of vaccinees		Seroprotection rate, % (95% CI)	Weight (common)	Weight (random
Non-endemic			ij			
Avelino-Silva et al (2016) ³⁵	21	24		– 88% (68–97)	1.7%	6.6%
de Melo et al (2011) ³⁶	20	20	<u> </u>	100% (83–100)	1.4%	6.3%
Bovay et al (2020) ³⁷	6	6	- !!	100% (54–100)	0.4%	3.8%
Lindsey et al (2020) ³⁰	519	546		95% (93–97)	37.8%	8.8%
Roukens et al (2018) ³²	73	75	<u> </u> -	97% (91–100)	5.2%	8.0%
Wieten et al (2016) ⁵⁸	91	99	-	92% (85–96)	6.9%	8.2%
Wieten et al (2016) ⁵⁷	13	14		93% (66–100)	1.0%	5.6%
Miyaji et al (2017) ⁵⁰	11	13	- il	- 85% (55-98)	0.9%	5.4%
Kareko et al (2020) ⁴⁸	24	38		63% (46–78)	2.7%	7.3%
Rosenstein et al (2021) ³¹	36	36	<u> </u>	100% (90–100)	2.5%	7.2%
Common-effect model		871		96% (94–97)	60.6%	
Random-effects model				94% (86–99)		67.2%
Heterogeneity: $I^2 = 77\%$, $\tau^2 = 0.0223$, χ^2_0	=38·45 (p<0	-0001)				
Endemic	,		11			
Campi-Azevedo et al (2016) ³⁸	65	84		77% (67–86)	5.8%	8.1%
Collaborative group for studies on	268	329	-	81% (77-86)	22.8%	8.7%
yellow fever vaccines (2014) ⁴¹			_			
Collaborative group for studies on	68	99		69% (59-78)	6.9%	8.2%
yellow fever vaccines (2019) ⁴²						
Campi-Azevedo et al (2019) ³⁹	39	55		71% (57-82)	3.8%	7.7%
Common-effect model		567	•	78% (74-81)	39.4%	
Random-effects model				76% (65–85)		32.8%
Heterogeneity: $I^2=65\%$, $\tau^2=0.0031$, $\chi^2=0.0031$	2=8·54 (p=0·0	0361)	ii ii			
Common-effect model	3	1438	i i	90% (88-92)	100.0%	
Random-effects model				89% (80-95)		100.0%
Heterogeneity: $I^2=90\%$, $\tau^2=0.0281$, $\chi^2=0.0281$	² ₁₂ =128·86 (p-	<0.0001)				
Test for subgroup differences (comm	_					
Test for subgroup differences (rando						
,	, n ₁	- 4 /				
	C	20 40	60 80	100		

(A) Proportion of healthy adults seroprotected in nonendemic and endemic settings

Schnyder JL et al. Lancet Glob Health 2024 Mar;12(3):e445e456

Conclusions

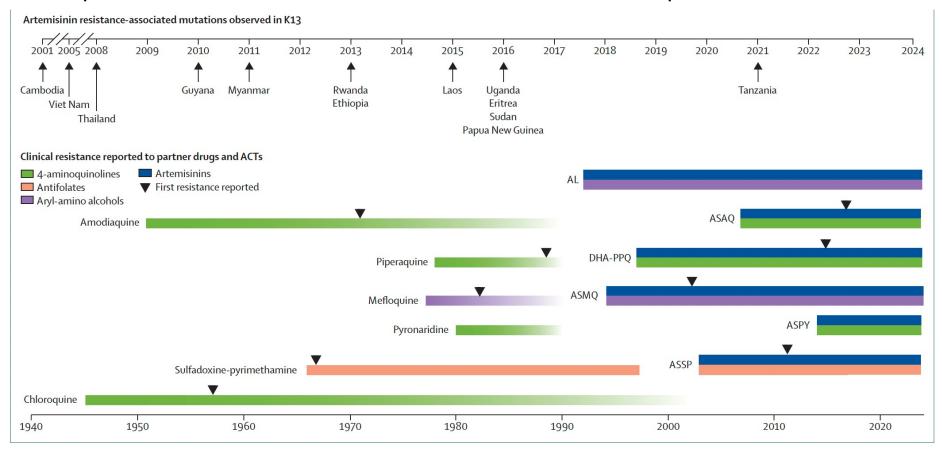
- Single dose YF vaccination provides lifelong protection in most travelers
- Persons living with HIV and children <2 years have lower seroprotection @10 years or more post-vaccination; booster may still be needed
- Lower seroprotection in endemic areas attributed to Brazil's higher cutoff for seroprotection



The emergence of artemisinin partial resistance in Africa: how do we respond? **Lancet Infect Dis. 2024 :S1473-3099(24)00141-5.**

Philip J Rosenthal, Victor Asua, Jeffrey A Bailey, Melissa D Conrad, Deus S Ishengoma, Moses R Kamya, Charlotte Rasmussen, Fitsum G Tadesse, Aline Uwimana, David A Fidock

- Partial resistance to artemisinin (ART-R) 1st reported in SE Asia 2008
- ART-R is mediated primarily by single point mutations in *P falciparum* kelch13 protein, with several mutations present in African parasites that are now validated resistance mediators per clinical and lab criteria



Lancet Infect Dis. 2024 :S1473-3099(24)00141-5.

The emergence of artemisinin partial resistance in Africa: how do we respond?

Philip J Rosenthal, Victor Asua, Jeffrey A Bailey, Melissa D Conrad, Deus S Ishengoma, Moses R Kamya, Charlotte Rasmussen, Fitsum G Tadesse, Aline Uwimana, David A Fidock

Antimalarial drug resistance in Africa

- Chloroquine in wide use since 1950s
- Resistance spread from SE Asia to Africa: 1st identified in Kenya 1979 but continued to be used
- Alternative= sulfadoxine-pyrimethamine, 1st used in Malawi 1993, +/- CQ or amodiaquine
- Early 21st Century: ACTs became standard of care

Additional concerns

- Resistance to ACT partner drugs
- Decreased parasite susceptibility to lumefantrine
- Efficacy low in Mekong region for
 - Artesunate-amodiaquine
 - Artesunate-mefloquine
 - Dihydroartemisinin-piperaquine
- Low A-L therapeutic efficacy reported: Angola,
 DRC, Burkina Faso, Uganda

ART-R emergence in Africa

- K13 mutations that are validated or candidate
 ART-R markers, increasing prevalence and spread in multiple regions, clinical and in vitro ART-R
- Rwanda K13 Arg561His: prevalence 20%, also in NW Tanzania
- Uganda K13 Cys469Tyr and Ala675Val: >30%
- Western Uganda: Pro441Leu and Cys469Phe
- Ethiopia and Eritrea Arg622Ile: prevalence 20%, also in Sudan

	WHO resistance marker status	Principal countries	Clinical evidence	In vitro evidence	
				Field samples	Transfected parasites
Pro441Leu	Candidate	Uganda	No	No	No
Cys469Phe	Candidate	Uganda	No	Yes	No
Cys469Tyr	Validated	Uganda	Yes	Yes	Yes
Arg561His	Validated	Rwanda, Tanzania, and Uganda	Yes	Yes	Yes
Arg622lle	Validated	Eritrea and Ethiopia	Yes	No	Yes
Ala675Val	Validated	Uganda	Yes	Yes	Yes

Lancet Infect Dis. 2024 :S1473-3099(24)00141-5.

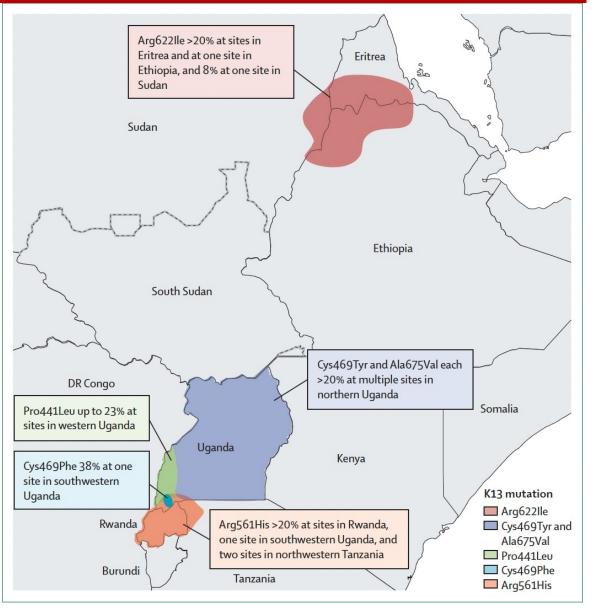
The emergence of artemisinin partial resistance in Africa: how do we respond?

Philip J Rosenthal, Victor Asua, Jeffrey A Bailey, Melissa D Conrad, Deus S Ishengoma, Moses R Kamya, Charlotte Rasmussen, Fitsum G Tadesse, Aline Uwimana, David A Fidock

Priorities in response to ART-R emergence in Africa

- Expand genomic surveillance for ART-R mutations across the continent
- More frequent testing of efficacies of artemisininbased regimens vs uncomplicated
- Study severe malaria in trials
- Assess ex-vivo antimalarial drug susceptibilities
- Change treatment policy to deter ART-R spread
- Accelerate development of new antimalarial regimens

ART-R emergence in Africa



Areas with prevalence >5% of indicated validated and candidate K13 mutations associated with ART-R







Journal of Travel Medicine, 2024, 1–8 https://doi.org/10.1093/jtm/taad165 Original Article

Original Article

Failure of artemether-lumefantrine therapy in travellers returning to Belgium with *Plasmodium falciparum* malaria: an observational case series with genomic analysis

Jan Pierreux, MD^{1,†,*}, Emmanuel Bottieau, MD, PhD^{2,†}, Eric Florence, MD, PhD³, Ula Maniewski, MD², Anne Bruggemans, MD², Jiska Malotaux, MD⁴, Charlotte Martin¹, MD, PhD¹, Janneke Cox, MD, PhD^{5,6}, Deborah Konopnicki, MD, PhD¹, Pieter Guetens, BSc⁷, Jacob Verschueren, MSc², Jasmine Coppens, PhD², Marjan Van Esbroeck, MD², Mathijs Mutsaers, MSc⁷ and Anna Rosanas-Urgell, PhD⁷

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- -Both early failure and late recrudescence have occurred.
- -Treatment successful with Malarone or more AL or artenimol-piperaquine or mefloquine...
- -some Belgian recrudescent cases received IV artesunate for severe malaria or while waiting for expert advice.



Journal of Travel Medicine, 2023, 1–9 https://doi.org/10.1093/jtm/taad114 Original Article

Original Article

Emergence of artemisinin-based combination treatment failure in patients returning from sub-Saharan Africa with *P. falciparum* malaria

Tamar Grossman¹, PhD Dr¹, Julia Vainer, MSc Dr¹, Yael Paran, MD^{2,3}, Liora Studentsky, MSc Dr¹, Uri Manor¹, MD Professor^{3,4}, Ron Dzikowski, PhD Professor⁵ and Eli Schwartz, MD, DTMH^{3,4}

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España-Cueto S et al. J Travel Med. 2023 Oct 31;30(6):taad030

Journal of Travel Medicine



Journal of Travel Medicine, 2023, 1– https://doi.org/10.1093/jtm/taad03 Original Articl

Results

Original Article

Post-infectious irritable bowel syndrome following a diagnosis of traveller's diarrhoea: a comprehensive characterization of clinical and laboratory parameters

Sergio España-Cueto, MD^{1,2,3}, Inés Oliveira-Souto, PhD^{1,4}, Fernando Salvador, PhD^{1,4,*}, Lidia Goterris, PhD⁵, Begoña Treviño, MD^{1,4}, Adrián Sánchez-Montalvá, PhD^{1,4}, Núria Serre-Delcor, PhD^{1,4}, Elena Sulleiro[®], PhD^{4,5}, Virginia Rodríguez, PhD⁵, Maria Luisa Aznar[®], PhD^{1,4}, Pau Bosch-Nicolau, MD^{1,4}, Juan Espinosa-Pereiro, MD^{1,4}, Diana Pou, MD^{1,4} and Israel Molina, PhD^{1,4}

Background

- GI symptoms can persistent after TD
- Study describe epidemiological, clinical, microbiologic characteristics of PI-IBS after tropics / subtropics

Methods

- International Health Barcelona: retrospective
- Patients seen 2009-2018 with PI-IBS: persistent or recurrent GI manifestations for >6 months after TD, negative bacterial stool culture & negative O&P after targeted treatment

- N= 669 with diagnosis of TD
- PI-IBS in 68 (10.2%)
- Mean age 33 years, 52.9% women
- Mean trip duration 30 days
- Most frequent areas visited: Latin America (29.4%),
 Middle East (17.6%)
- Microbiological diagnosis of TD in 47%: 75%
 parasitic, Giardia duodenalis most common (83.3%)
- Symptoms lasted a mean of 15 months after TD
- Endoscopy: 35% abnormal: gastritis/UC/ diverticulosis, polyp, hemorrhoids
- Parasitic infections independent risk factors: OR 3.0
- Pre-travel counselling reduced PI-IBS: OR 0.4

Conclusions

- 10% of patients with TD developed PI-IBS
- Parasitic infections associated with PI-IBS (giardiasis)

Post-infectious irritable bowel syndrome following a diagnosis of traveller's diarrhea: a comprehensive characterization of clinical and laboratory parameters.

Espana-Cueto S et al. J Travel Med. 2023 Oct 31;30(6): taad030.

Table 2. Characterization of the episode of TD preceding the development of PI-IBS

		n = 68
Gender	Male	32 (47.1%)
	Female	36 (52.9%)
Mean age (in years)		33 (SD 10.6)
Purpose of the travel	Tourism	45 (66.2%)
	VFR	11 (16.2%)
	Work	7 (10.3%)
	Cooperation	5 (7.4%)
Geographical areas	Latin America	20 (29.4%)
visited	Middle East	12 (17.6%)
	Oceania and South-East	12 (17.6)
	Asia	
	Sub-Saharan Africa	7 (10.3)
	North Africa	6 (8.8%)
	Unknown	11 (16.2%)
Median duration of		30 (IQRS 14-96)
the trip (in days)		
Median duration of		30 (IQR 12-120)
symptoms (in days)		
Mean number of		6 (SD 3.9)
bowel movements		
per day		
Symptoms onset	During the trip	49 (72.1%)
	After the trip	19 (27,9%)
Clinical picture	Abdominal pain	46 (32.4%)
	Fever	28 (41.2%)
	Dysentery	22 (32.4%)
	Nausea	20 (29.4%)
	Vomiting	14 (20.6%)
Aetiology	Parasitic infection	24 (35.3%)
87	Bacterial infection	6 (8.8%)
	Mixed infection	2 (2.9%)
	Unknown	36 (52.9%)
Parasites and protists	Giardia duodenalis	20 (29.4%)
detected	Blastocystis spp.	6 (8.8%)
	Entamoeba histolytica	2 (2.9%)
	Dientamoeba fragilis	3 (4.4%)
Bacteria detected	Enteropathogenic	3 (4.4%)
Ductoria detected	Escherichia coli	0 (11170)
	Enteroinvasive E. coli	3 (4.4%)
	Enterotoxigenic E. coli	2 (2.9%)
	Shigella spp.	2 (2.9%)

Table 3. Characteristics of individuals presenting with PI-IBS responding a questionnaire via a follow-up telephone call

		n = 43
Mean time of remaining		15 (SD 6-18)
symptoms (in months)		
Persistent symptoms	Change in the frequency	12/43 (27.9%)
	and/or consistency of	
	bowel movements	
	Intermittent abdominal	11/43 (25.6%)
	pain	
	Flatulence	7/43 (16.3%)
Concomitant chronic	Yes	31/43 (72.1%)
treatment	No	12/43 (27.9%)
Impairment in activities	No	2/43 (4.7%)
of daily living	Slight	11/43 (25.6%)
	Moderate	18/43 (41.9%)
	Severe	12/43 (27.9%)
Gastroenterologist	Yes	17/43 (39.5%)
evaluation	No	26/43 (60.5%)
Endoscopic examination	Yes	20/43 (46.5%)
performed	No	23/43 (53.5%)
Abnormalities upon	No abnormalities	13/20 (65%)
endoscopic examination	Gastritis	2/20 (10%)
	Ulcerative colitis	2/20 (10%)
	Diverticulosis	1(20) (5%)
	Polyposis	1/20 (5%)
	Haemorrhoids	1/20 (5%)
Specific counselling of	Yes	28/43 (65.1%)
symptomatic treatment	No	15/43 (34.9%)
New trips	Yes	28/43 (65.1%)
	No	15/43 (34.9%)
New diagnosis of TD	Yes	6/28 (21.4%)
after the new trip	No	22/28 (78.6%)
Risk score for PI-IBS	Low	10/43 (23.8%)
	Moderate	29/43 (69%)
	High	3/43 (7.1%)

During-travel



Maier JD et al. J Travel Med. 2023 Dec 28;30(8):taad117.





Journal of Travel Medicine, 2023, 1–9 https://doi.org/10.1093/jtm/taad117 Original Article

Original Article

The Ready-To-Go Questionnaire predicts health outcomes during travel: a smartphone application-based analysis

Julian D. Maier¹, MD^{1,*}, Alexia Anagnostopoulos, MD MPH¹, Anna Gazzotti, MD¹, Silja Bühler, MD MSc², Vasiliki Baroutsou, MSc¹, Christoph Hatz, MD^{1,3,4}, Milo A. Puhan, MD PhD⁵, Jan Fehr, MD^{1,†} and Andrea Farnham, PhD^{1,†}

Background

Assessed R2G in identifying high-risk travellers, predicting health events/behaviour during travel in TOURIST2 cohort

Methods

- TOURIST2: 1000 participants enrolled 2017-2019, daily smartphone app surveys pre-during-post travel
- Used TOURIST2 data to calculate medical/travel risk scores, categorize each participant based on risk
- Regression models to analyse incidence of overall health events and grouped into respiratory/GI/injury

Results

- N=793, 54.5% female, median age 34 y
- Mean trip= 16.0 days, tourism 78.7%
- 83% with risk for health events, 17% high risk
- R2G high-risk travellers correlated with incidence of health events (high-risk vs lowerrisk IRR=1.27)
 - -Medical events IRR=1.11 (GI, resp, myalgia, mental health)
 - -Travel events IRR=1.07
- Chronic health conditions:
 - -Accessed medical care more often (IRR=1.16),
 - -Had greater difficulty carrying out planned activities (IRR=-0.04),
 - -Rated travel experience lower (IRR=-0,04)
- Increased travel-related risks (planned itinerary): more frequent animal contact (IRR=1.09), injury (IRR=1.28)

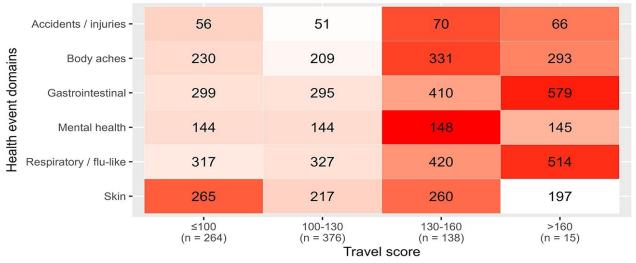
Results

Heat maps showing IRs per 1000 travel days for each health event domain in different medical or travel score

Maier JD et al. J Travel Med. 2023 Dec 28;30(8):taad117.

- Farnham A et al. Travel Med Infect Dis. 2022;47:102294.
- Baroutsou V et al. Travel Med Infect Dis. 2021;39:101912.
- Gazzotti A et al. Travel Med Infect Dis. 2022;47:102304.





Results

Association of R2G scores (predictor) and incidence of health events (outcome)

References: destination Tanzania (lowest incidence of health events), purpose tourism (most common purpose)

Conclusions

- High medical risk travellers more likely to be VFR, travel for longer periods, suggest an association between chronic medical conditions and VFR.
- R2G: incorporate into pre-consultation triage for travellers to self-identify their risk level

Maier JD et al. J Travel Med. 2023 Dec 28;30(8):taad117.

Predictors	IRR (95% CI)	<i>P</i> -value
R2G Medical Risk Score	1.11 (1.07–1.16)	<0.001*
R2G Travel Risk Score	1.07 (1.03–1.12)	0.002*
Age	0.98 (0.97-0.98)	<0.001
Sex (female=1)	1.13 (1.00-1.28)	0.056
Planned trip duration	1.00 (0.99–1.00)	0.480
Destination Brazil	1.20 (0.98–1.47)	0.069
Destination China	1.73 (1.21–2.51)	0.003*
Destination India	1.58 (1.27–1.96)	<0.001
Destination Peru	1.39 (1.12–1.72)	0.003*
Destination Thailand	1.47 (1.09–1.97)	0.009*
Travel Purpose: Business	0.91 (0.71–1.19)	0.490
Travel Purpose: Other	0.94 (0.54–1.79)	0.836
Travel Purpose: Study	1.47 (0.88–2.62)	0.161
Travel Purpose: VFR	0.91 (0.72–1.15)	0.419
Travel Purpose: Volunteer Work	0.76 (0.55–1.07)	0.106

Wilderness Medical Society Clinical Practice Guidelines on Water Treatment for Wilderness, International Travel, and Austere Situations: 2024 Update

Wilderness & Environmental Medicine 2024, Vol. 35(1S) 45S-66S © Wilderness Medical Society 2023 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/10806032231218722 www.wemjournal.org



Howard D. Backer, MD, MPH¹, Robert W. Derlet, MD², and Vincent R. Hill, PhD³





Journal of Travel Medicine, 2024, 1–13 https://doi.org/10.1093/jtm/taad088 Review

Review

Injuries and medical emergencies among international travellers

Mathieu Potin[®] MD^{1,*}, Pierre-Nicolas Carron MD² and Blaise Genton MD, PhD³

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Summary

Pre-travel

- AI can provide basic uncontextualized pre-travel advice, but still need TM providers' finesse
- Updated VPD epidemiology help to prioritize vaccination based on incidence, seriousness/sequelae

Vaccines

- Chikungunya: live-attenuated vaccine single dose achieves robust immune response: available in US
- Dengue: TAK-003 recommendations; 3rd live-attenuated vaccine achieved VE 80% in dengue-naïve/90% in those with prior dengue
- Rabies: results from study on boostability following 1-dose PrEP reassuring re 2-dose PrEP
- Yellow fever: duration of protection revisited, young children and PLWH need revaccination

Summary 2

- Malaria
 - Emergence of partial artemisinin resistance in Africa calls for response including genomic surveillance, test for efficacy, ex-vivo test of drug susceptibility, change treatment
- GI/travellers' diarrhea/Post-travel
 - PI-IBS associated with parasitic infection, mainly Giardia
- During-travel:
 - Ready-To-Go Questionnaire scores predict health outcome

Zika virus infection in European travellers returning from Thailand in 2022: A GeoSentinel case series

Davidson H. Hamer ^{3,4,5} Timothy Seers 1 Camilla Rothe² Sarah Denny¹ Rahel Spindler² Eli Schwartz⁶ Victoria Johnston 1,7

RAPID COMMUNICATION

A cluster of autochthonous dengue transmission in the Paris region - detection, epidemiology and control measures, France, October 2023

Nelly Fournet¹, Nathalie Voiry², Julian Rozenberg², Clément Bassi³, Caroline Cassonnet³, Anaïs Karch⁴, Guillaume Durand^{5,6}, Gilda Grard^{5,6}, Gabriela Modenesi¹, Stevens-Boris Lakoussan¹, Nicolas Tayliam⁷, Marta Zatta⁸, Sébastien Gallien⁸, on behalf of the investigation team⁹, Harold Noël¹⁰, Ségolène Brichler^{11,*}, Arnaud Tarantola^{1,*} 1. Santé publique France (French National Public Health Agency), Saint-Denis, France

Centers for Disease Control and Prevention



Morbidity and Mortality Weekly Report

April 11, 2024



Epidemiological Alert Oropouche in the Region of the Americas 9 May 2024

Contents lists available at ScienceDirect



journal homepage: www.elsevier.com/locate/tmaid





Safety and efficacy of malaria vaccine candidate R21/Matrix-M in African children: a multicentre, doubleblind, randomised, phase 3 trial



Mehreen S Datoo, Alassane Dicko*, Halidou Tinto*, Jean-Bosco Ouédraogo, Mainga Hamaluba†, Ally Olotu†, Emma Beaumont, Fernando Ramos Lopez, Hamtandi Magloire Natama, Sophie Weston, Mwajuma Chemba, Yves Daniel Compaore, Djibrilla Issiaka, Diallo Salou, Athanase M Some, Sharon Omenda, Alison Lawrie, Philip Bejon, Harish Rao, Daniel Chandramohan, Rachel Roberts, Sandesh Bharati, Lisa Stockdale, Sunil Gairola, Brian M Greenwood, Katie J Ewer‡, John Bradley, Prasad S Kulkarni, Umesh Shaligram, Adrian V S Hill, the R21/Matrix-M Phase 3 Trial Group§



Detection of Anopheles stephensi Mosquitoes by Molecular Surveillance, Kenya

Eric O. Ochomo, Sylvia Milanoi, Bernard Abong'o, Brenda Onyango, Margaret Muchoki, Diana Omoke, Evelyn Olanga, Laban Njoroge, Elijah Omondi Juma, James Dan Otieno, Damaris Matoke-Muhia, Luna Kamau, Cristina Rafferty, John E. Gimnig, Mildred Shieshia, Daniel Wacira, Joseph Mwangangi, Marta Maia, Charles Chege, Ahmeddin Omar, Martin K. Rono, Lucy Abel, Wendy Prudhomme O'Meara, Andrew Obala, Charles Mbogo, Lenson Kariuki

Human rabies despite post-exposure prophylaxis: a systematic review of fatal breakthrough infections after zoonotic exposures



Erin RWhitehouse, Anna Mandra, Jesse Bonwitt, Erin A Beasley, Joanna Taliano, Agam K Ra



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environmental

Review article

Antibiotic resistance monitoring in wastewater in the Nordic countries: A systematic review



Ananda Tiwari a,*, Adriana Krolicka b, Tam T. Tran b, Kati Räisänen c, Ásta Margrét Ásmundsdóttir^d, Odd-Gunnar Wikmark ^{b,e}, Rolf Lood ^f, Tarja Pitkänen ^{a,g,**}



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