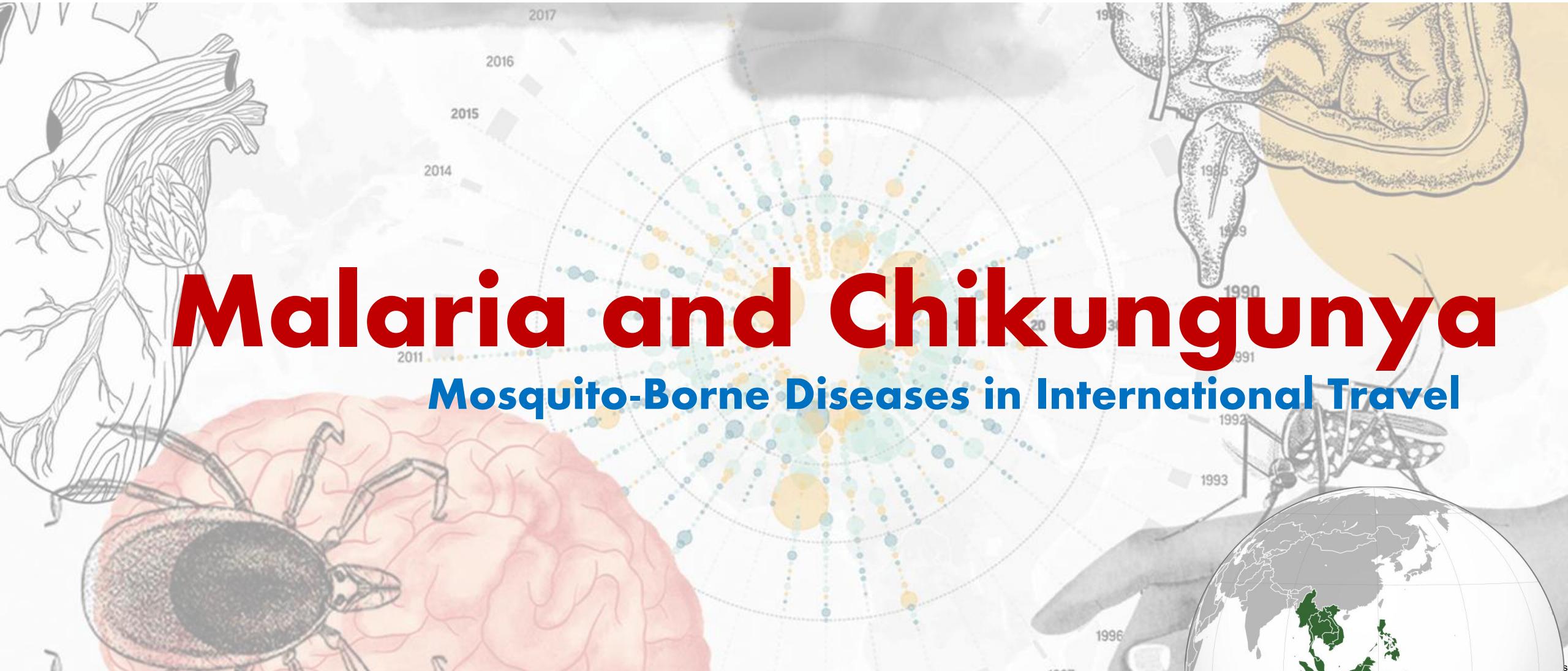




Malaria and Chikungunya

Mosquito-Borne Diseases in International Travel

Dr. Wasin Matsee, MD, MCTM, Dip. Board Travel Med, CTH®

Travel Medicine Research Unit, Department of Clinical Tropical Medicine

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Thai Travel Clinic, Hospital for Tropical Diseases, Bangkok, Thailand





Conflict of Interest

- Grants / Research support: Sanofi Pasteur
- Speakers' bureau or advisory board memberships: Sanofi Pasteur, Takeda, GSK, MSD, BioNet Asia



LEARNING OBJECTIVES

- At the conclusion of this presentation, learners will be able to:
 - Epidemiology of malaria and chikungunya in international travelers
 - Preventive measures for malaria and chikungunya in travelers



Thai Travel Clinic
Hospital for Tropical Diseases
Faculty of Tropical Medicine, Mahidol University



International Society of Travel Medicine
Promoting healthy travel worldwide
Established 1991

Journal of Travel Medicine, 2020, 1–3

doi: 10.1093/jtm/taaa015

Editorial

Editorial

Travellers give wings to novel coronavirus (2019-nCoV)

Key words: Wuhan, SARS, MERS, novel coronavirus, bats, live animal markets, spillover, cross-species spread, respiratory, airborne, one health, super-spreader

“Travelers play an important role for international spreading”

- Human to human esp. respiratory virus



COVID-19 and travel: International Spread

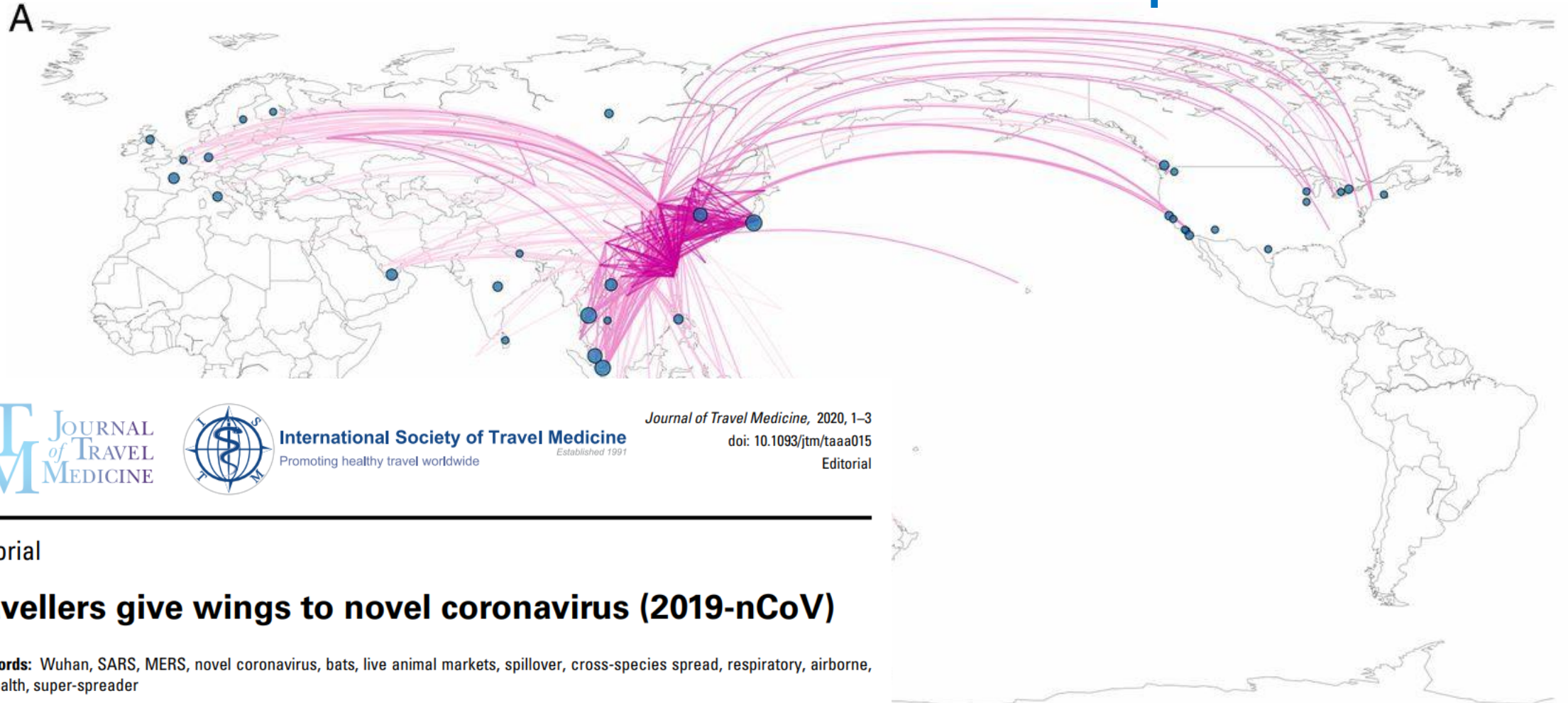




Table 2. Diagnosis According to Syndrome Group and Travel Region among Ill Travelers Returning from the Developing World.*

Diagnosis	All Regions (N=17,353)	Caribbean (N=1115)	Central America (N=1326)	South America (N=1675)	Sub-Saharan Africa (N=4524)	South Central Asia (N=2403)	Southeast Asia (N=2793)	Other or Multiple Regions (N=3517)†
<i>number of cases per 1000 patients</i>								
Systemic febrile illness‡	226	166	153	143	371	171	248	145
Acute diarrhea‡	222	196	234	219	167	327	210	238
Dermatologic disorder‡	170	261	225	264	127	130	212	125
Chronic diarrhea‡	113	132	173	130	57	129	97	149
Nondiarrheal gastrointestinal disorder‡	82	87	75	82	70	74	58	121
Respiratory disorder‡	77	45	49	50	77	89	97	86
Nonspecific symptoms or signs‡	70	53	51	59	75	85	63	77
Genitourinary disorder‡	35	29	11	27	51	25	29	40
Asymptomatic parasitic infection‡	30	15	26	33	29	44	30	24
Underlying chronic disease‡	19	14	23	18	20	14	13	27
Injury‡	14	23	11	14	7	15	14	21
Neurologic disorder‡	15	23	24	16	10	15	10	16
Adverse drug or vaccine reaction‡	12	4	5	5	26	12	8	8
Psychological disorder‡	12	8	20	15	8	12	10	18
Tissue parasite‡	10	5	5	11	22	4	3	7
Cardiovascular disorder	8	12	7	5	8	7	5	10
Obstetrical or gynecologic disorder	3	3	2	2	4	3	3	3
Ophthalmologic disorder	2	2	2	2	2	1	1	2
Dental problem	1	1	1	1	1	0	2	1
Death	1	1	0	0	1	3	0	1
Loss to follow-up‡	8	9	12	9	8	5	4	13

* Diagnoses included in each syndrome category are listed in the Supplementary Appendix. Numbers may not total 1000 because patients may have had more than one diagnosis.

† This category includes travel to West Asia, Northeast Asia, eastern Europe, Oceania, North Africa, or Antarctica (1868 travelers) or to multiple developing regions, for which ascertainment of exposure was impossible (1649 travelers).

‡ P<0.01 for the comparison among regions.

Diagnosis According to Syndrome Group and Travel Region among Ill Travelers Returning from the Developing World



Ill-returned Travelers

- Fever is one of the most common reported symptom among ill-returned travelers
- May lead hospitalization and life-threatening illness
- 28% of 24,920 ill travelers presented with fever at travel clinic on their return home¹

¹Wilson ME, et al. Clin Infect Dis.2007;44:1560-8.



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Journal of Travel Medicine, 2020, 1–12

doi: 10.1093/jtm/taaa207

Advance Access Publication Date: 4 November 2020

Original Article

Original Article

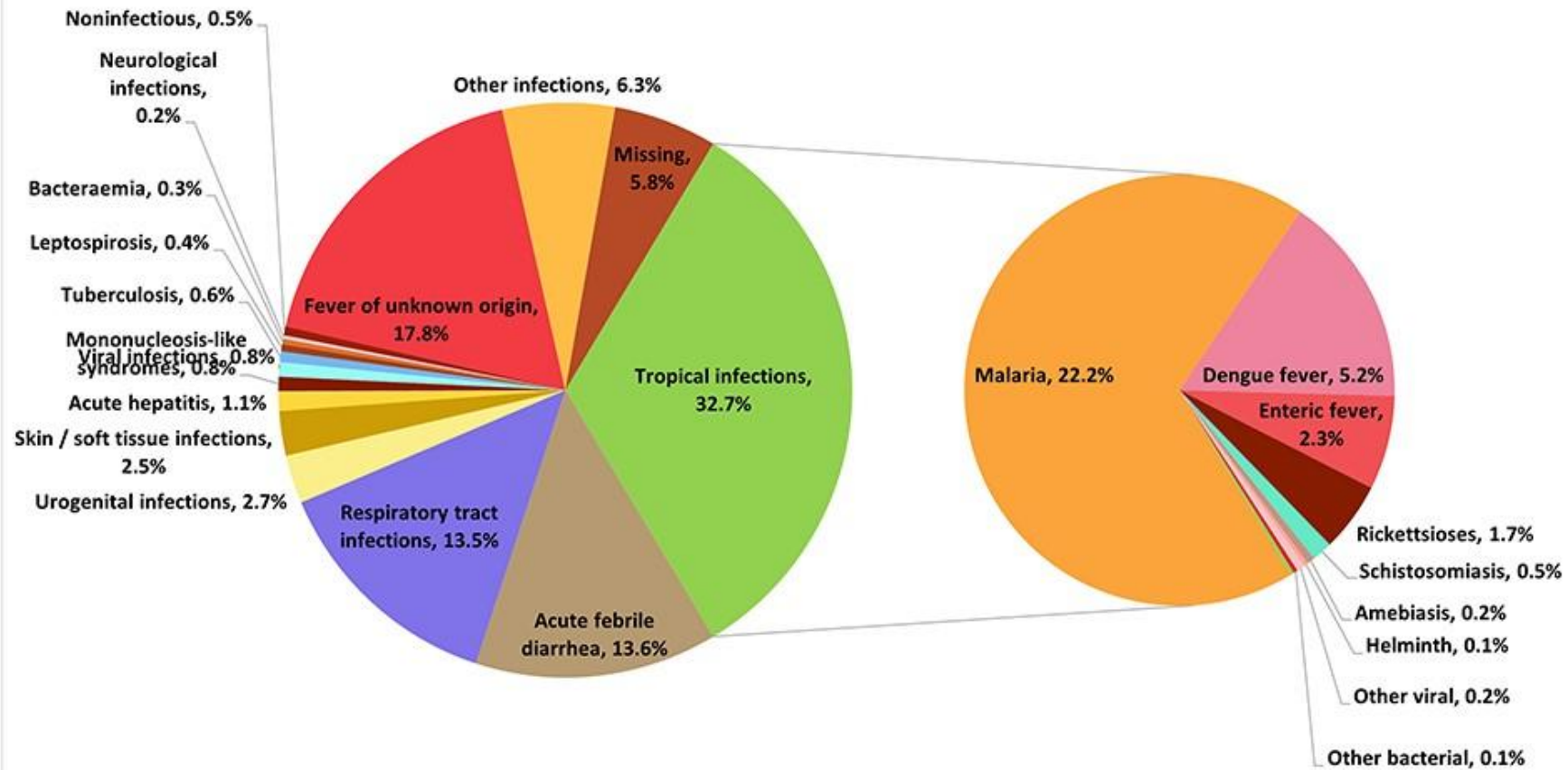
Aetiology of fever in returning travellers and migrants: a systematic review and meta-analysis

**Imogen Buss MBChB, MScGH, EADTMH¹, Blaise Genton MD, PhD^{1,2,*} and
Valérie D'Acremont MD, PhD^{1,2}**

¹Centre for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland and ²Swiss
Tropical and Public Health Institute, University of Basel, Basel, Switzerland

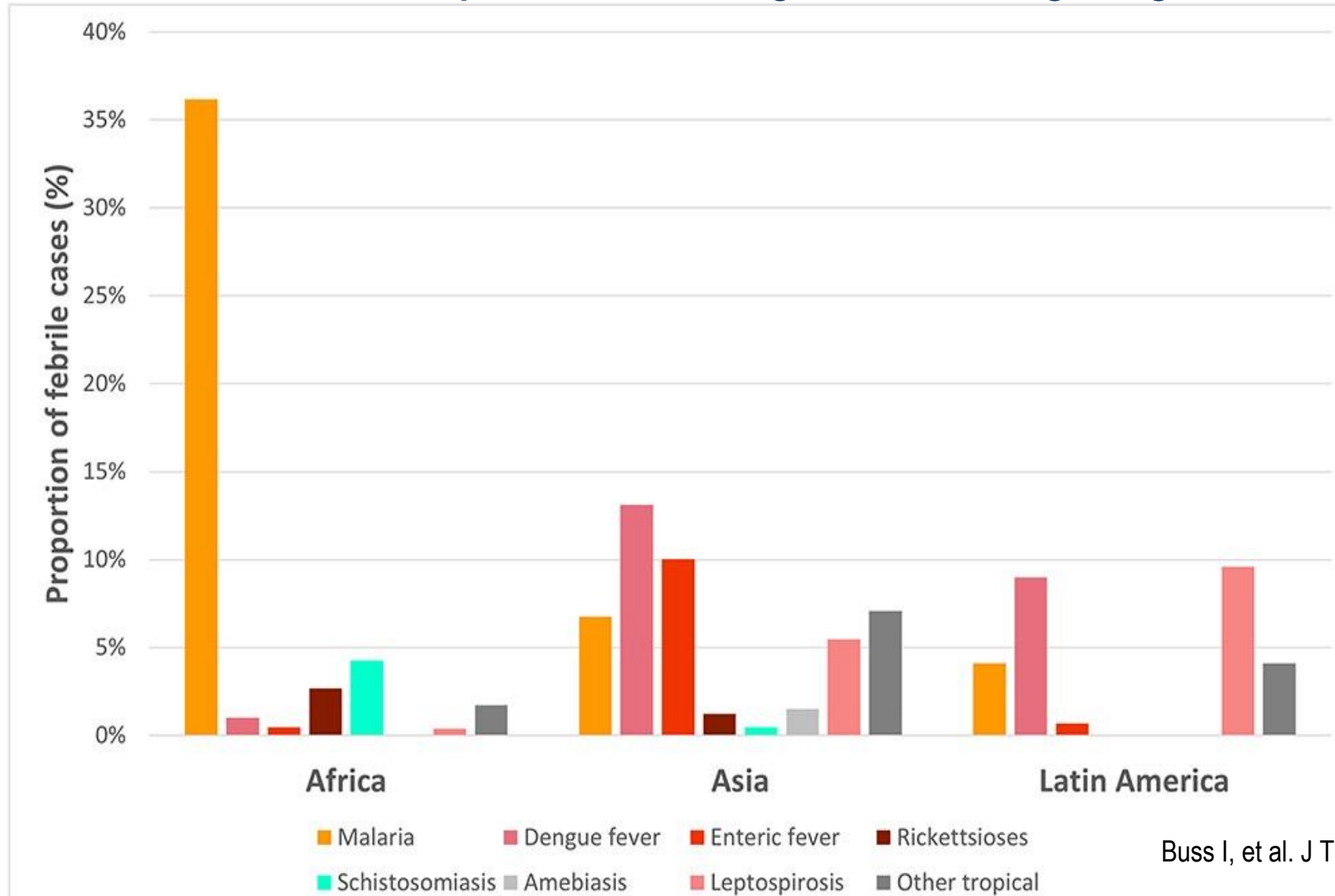


ETIOLOGY IN FEBRILE RETURNING TRAVELERS AND MIGRANTS





Prevalence of common tropical diseases categorized according to region visited





Fever in Returned Travellers: Challenges

• Diseases:

- Common causes in different region is different
- Most tropical diseases share similar presentation (challenges in diagnosis)
- Emerging of new infection: Mpox, Oropouche, many more ...

• Clinician:

- Unfamiliar with the endemic diseases (required specialists)
- Miss the history of exposure/travel history
- Delayed diagnosis and treatment



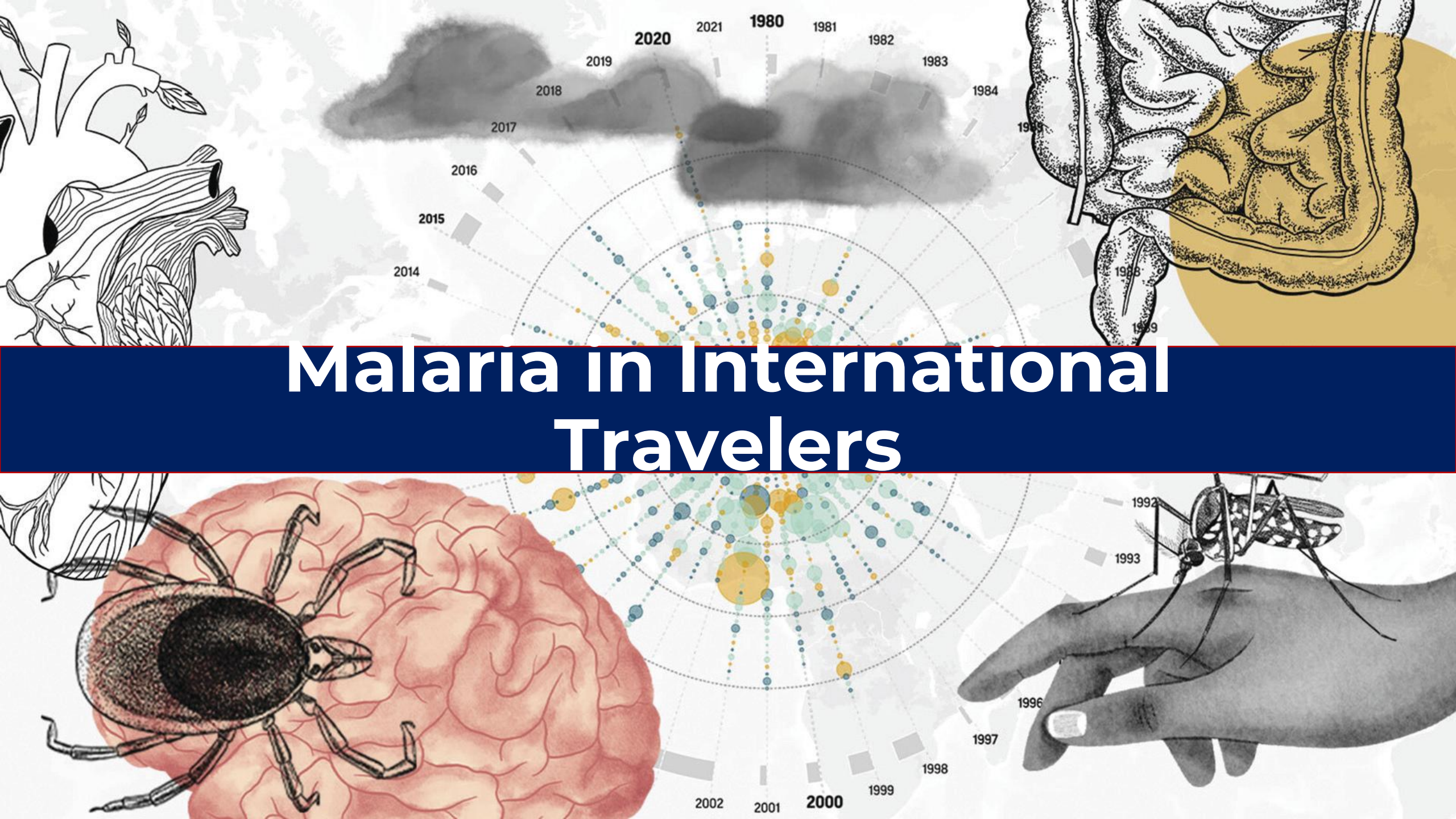


Fever in Returned Travellers: Challenges

- **Patients (Travelers):**
 - Unaware of risk esp. malaria
 - Delayed presentation

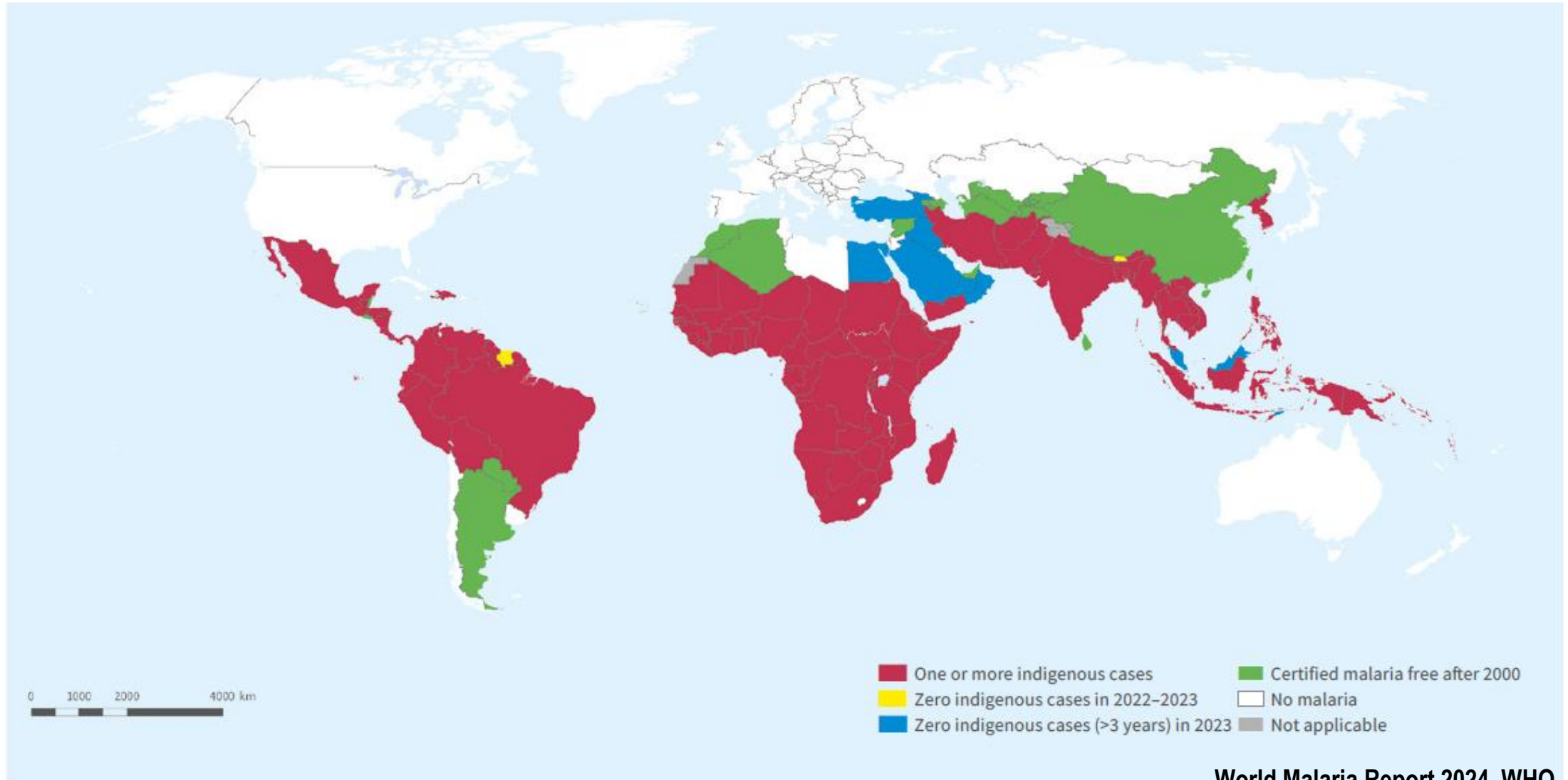


Malaria in International Travelers





Global Burden of Malaria





Introduction

- Most serious, life-threatening infectious caused by protozoan pathogens - *Plasmodium* spp.
- 263 million malaria cases including **597,000 malaria deaths** worldwide in 2023
- > 95% deaths occurred in Africa (**>50% - Children age < 5yrs**)
- **> 30,000 travel-related malaria cases** are reported annually
- Common cause of fever in returning travelers (esp. Sub-Saharan Africa)
- Hongkong is non-endemic for malaria
- More than 20 cases imported annually

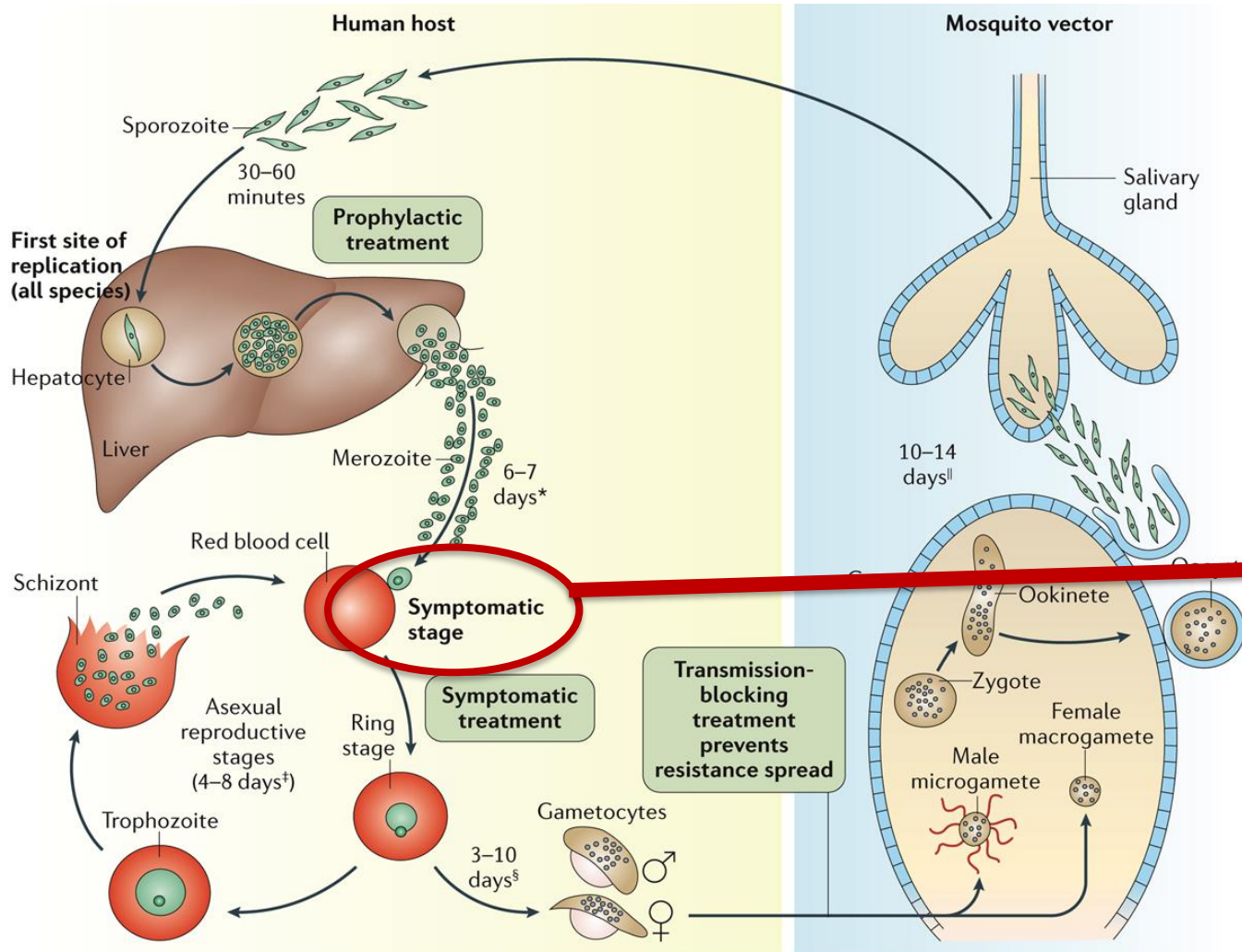


Introduction

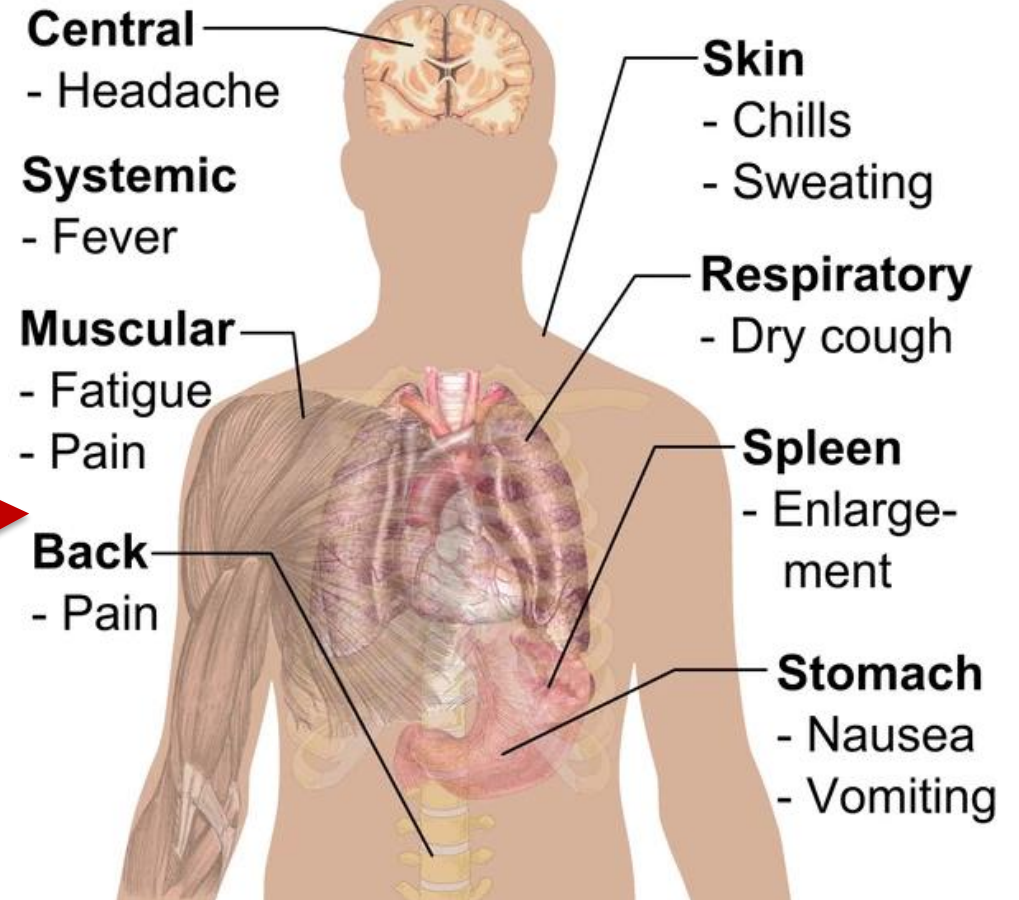
- 5 *Plasmodium* spp. can cause human malaria
 - *P. falciparum* – predominantly in Africa
 - *P. vivax* – Asia and South Americas
 - *P. malariae*
 - *P. ovale*
 - the simian parasite *P. knowlesi* - the island of Borneo but has been reported in other South-East Asian countries



The *Plasmodium* spp. life cycle



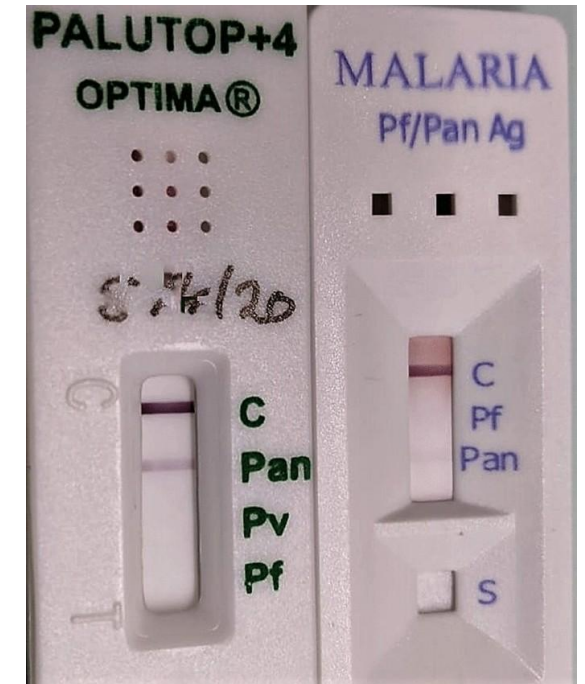
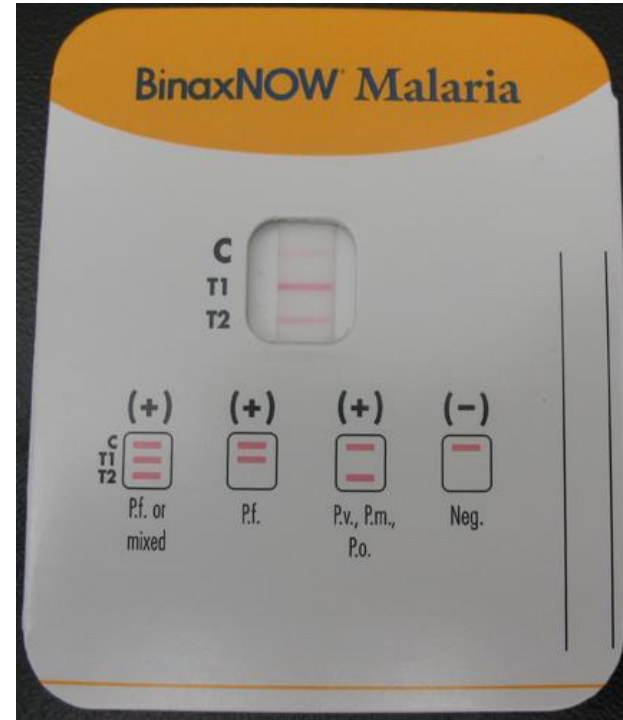
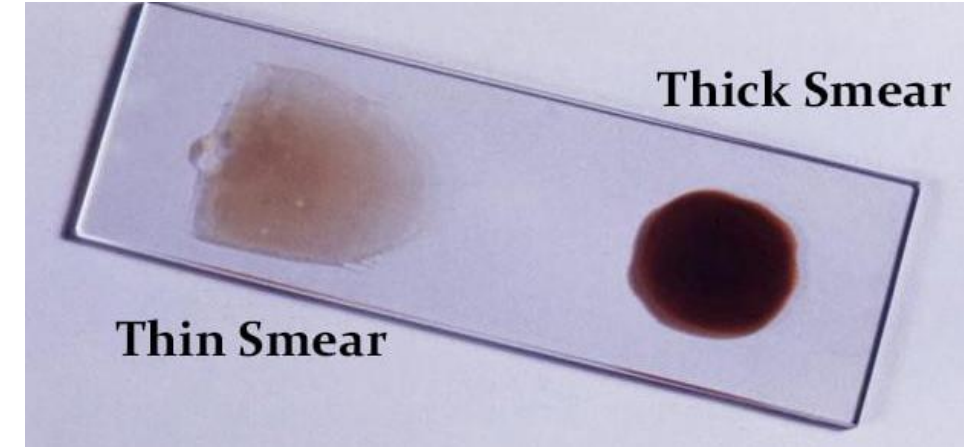
Symptoms of Malaria





Diagnostic test

- Microscopy (Thick/Thin film) – Gold standard
- Rapid antigen test
- Molecular method (PCR)





Common pitfall of travel-related malaria deaths



Delay diagnosis and delay treatment*

(Malaria is 100% treatable! Early diagnosis and prompt treatment is the key!)



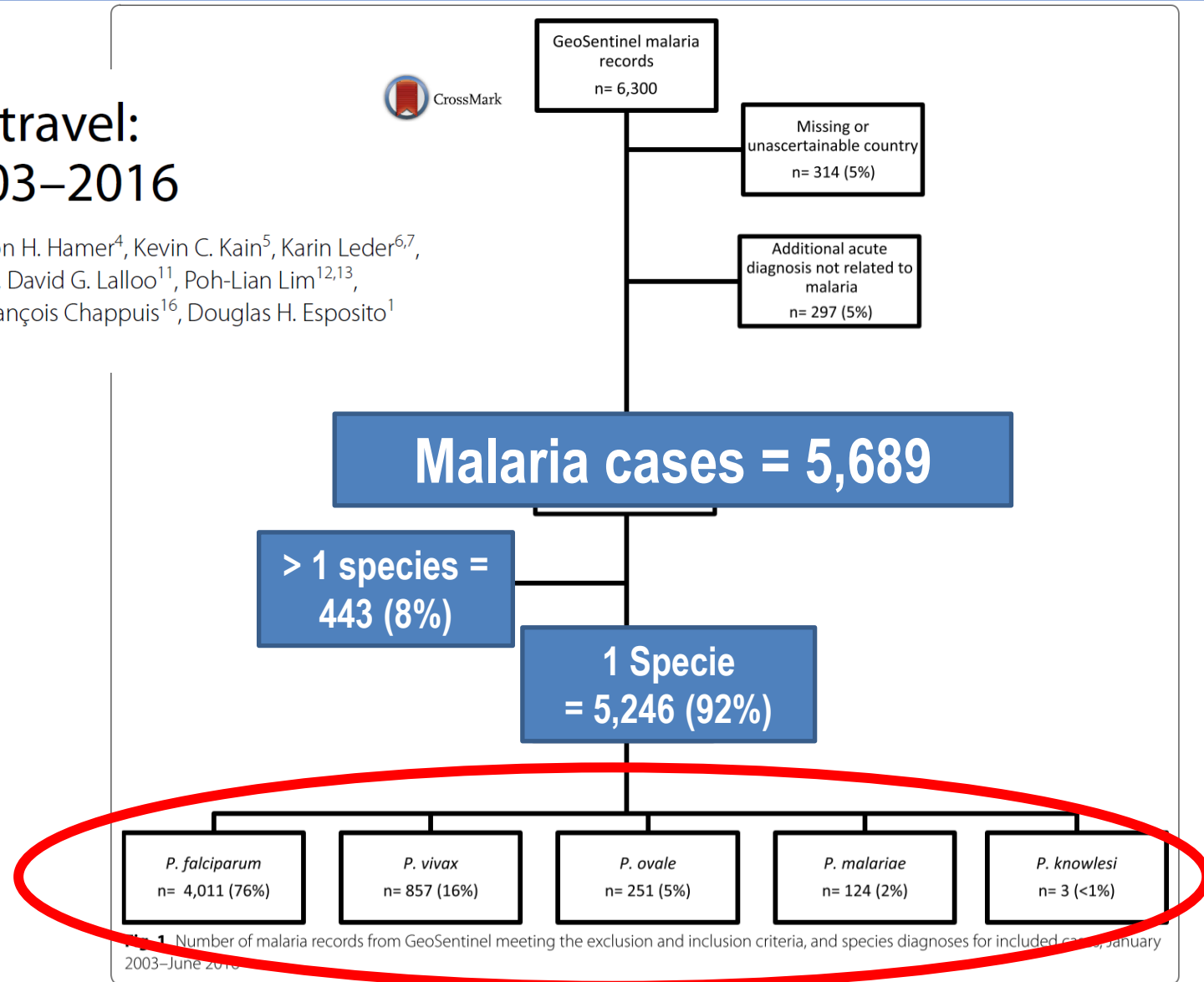
Common Cause of Fever in Returned Travelers

Sub-Saharan Africa	Southeast Asia	Caribbean and Central and South America
Malaria 42%	Dengue 18%	Diarrheal illness 15%
Respiratory illness 10%	Respiratory illness 17%	Respiratory illness 13%
Diarrheal illness 10%	Diarrheal illness 17%	Dengue 9%
Other system febrile illness 7%	Malaria 7%	Malaria 8%
No diagnosis 19%	Other systemic febrile illness 9%	Other systemic febrile illness 8%
	No diagnosis 22%	No diagnosis 26%



Malaria after international travel: a GeoSentinel analysis, 2003–2016

Kristina M. Angelo^{1*}, Michael Libman², Eric Caumes³, Davidson H. Hamer⁴, Kevin C. Kain⁵, Karin Leder^{6,7},
Martin P. Grobusch⁸, Stefan H. Hagmann⁹, Phyllis Kozarsky^{1,10}, David G. Lalloo¹¹, Poh-Lian Lim^{12,13},
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and for the GeoSentinel Network

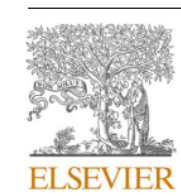




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and for the GeoSentinel Network

- 53% were **VFRs**
- 60% of travelers with *P. falciparum*
- Median trip duration was **32 days** (IQR range 20-75 days)
- More than 40% of travelers with a trip duration ≤ 7 days had *P. vivax*
- Median days between return and presenting to a site **11 days** (IQR range 6-21 days)
- 62% were hospitalized (8% severe, 12 travelers died)



Epidemiologic trends and clinical outcomes of imported malaria in a tertiary care hospital, Bangkok, Thailand: A retrospective analysis (2013–2022)

Panita Looareesuwan^{a,b}, Rachata Charoenwisetsil^b, Punyisa Asawapaithulsert^b,
Phimphan Pisutsan^{b,c}, Viravarn Luvira^c, Watcharapong Piyaphanee^{b,c}, Wasin Matsee^{b,c,*}

Figure 1 Transnational and border malaria in a tertiary hospital, Bangkok, Thailand (2013–2022)

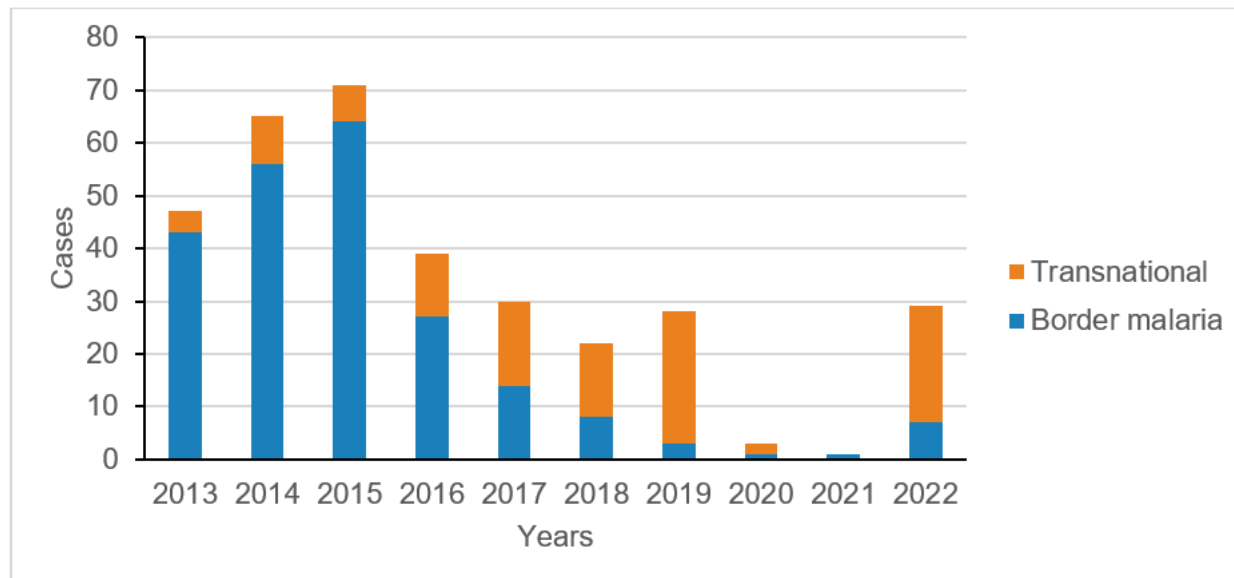


Table 2

Demographic, clinical and treatment outcomes of imported malaria according to severity of illness.

Characteristics	Uncomplicated malaria N = 294	Severe malaria ^a N = 41	Total
Sex, n = 335 (%)			
Female	37 (12.6)	12 (29.3)	49 (14.6)
Male	257 (87.4)	29 (70.7)	286 (85.4)
Median age, n = 335 (IQR),	28 (21–36)	34 (25–47)	
Nationality, n = 335 (%)			
Thai	57 (19.4)	10 (24.4)	67 (20)
Asian (non-Thai) ^b	187 (63.6)	22 (53.7)	209 (62.4)
African	39 (13.3)	5 (12.2)	44 (13.1)
European and others ^c	11 (3.7)	4 (9.8)	15 (4.5)
Occupation, n = 307 (%)			
Unskilled labour	187 (69.5)	24 (63.2)	211 (68.7)
Professionals ^d	25 (9.3)	6 (15.8)	31 (10.1)
Merchant	27 (10.0)	3 (7.9)	30 (9.8)
Others	30 (11.2)	5 (13.2)	35 (11.4)
Purpose of travel, n = 322 (%)			
Visiting friends and relatives	201 (71.5)	26 (63.4)	227 (70.5)
Business/occupational	52 (18.5)	12 (29.3)	64 (19.9)
Tourism	25 (8.9)	3 (7.3)	28 (8.7)
Others ^e	3 (1.1)	0 (0.0)	3 (0.9)
Country/region of acquisition, n = 335 (%)			
Sub-Saharan Africa	76 (25.9)	19 (46.3)	95 (28.4)

Plasmodium knowlesi in HTD (2022)

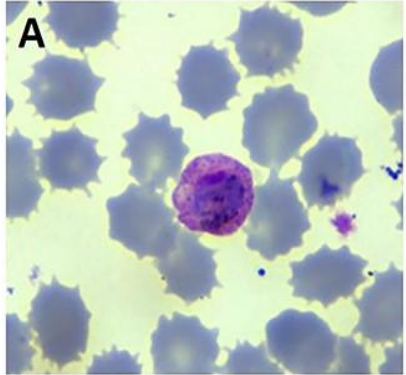
Case	Chief complaint	Diagnosis	Status
1	60-year-old Thai male referred to HTD with severe <i>P. falciparum</i> malaria	<i>P. Knowlesi</i> (from Kanchanaburi)	ICU, Recovery
2	71-year-old male Thai with U/D HT,DLP referred to HTD with severe <i>P. falciparum</i> malaria	<i>P. Knowlesi</i> (from Ratchaburi)	ICU, Recovery
3	61-year-old male Thai U/D HT,DM referred to HTD with severe <i>P. falciparum</i> malaria	<i>P. Knowlesi</i> (from Satun)	ICU, Recovery

Practical consideration

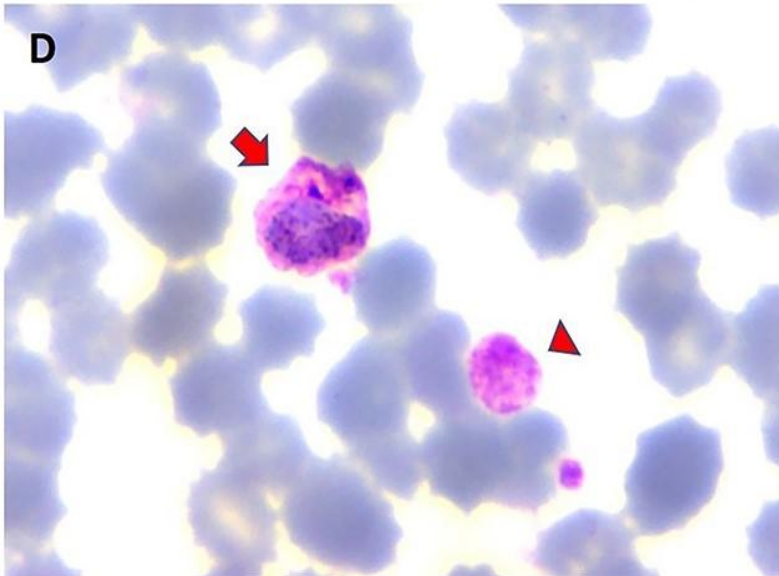
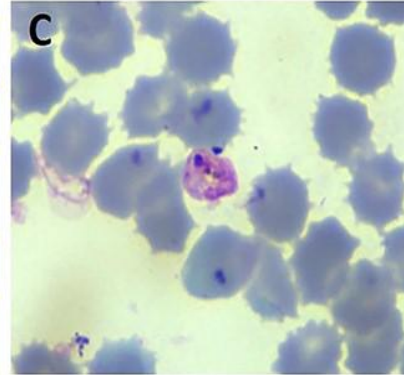
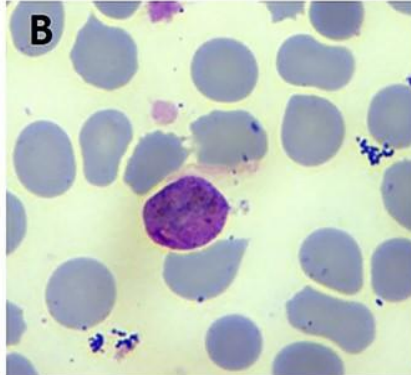
- Severe *P. knowlesi* infection can resemble *P. falciparum*, making differentiation challenging using microscopy >> cases may underreported.
- Delayed diagnosis >> lead to severe malaria (lack of travel history)
- Severe *P. knowlesi* infection: Present with clinical severity despite low parasitemia



Plasmodium vivax



Plasmodium knowlesi



Clinical Pearls

Challenges of *Plasmodium vivax* and *Plasmodium knowlesi* co-infection

Rachata Charoenwisedsil, MD^{1,2}, Punyisa Asawapaithulsert, MD^{1,2},
Phimphan Pisutsan, MD^{1,2}, Kesinee Chotivanich, PhD^{1,2} and Wasin Matsee, MD^{1,2,*}

¹Thai Travel Clinic, Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand and ²Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

*To whom correspondence should be addressed. Travel Medicine Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, 420/6 Ratchawithi Road, Bangkok 10400, Thailand. Email: wasin.mat@mahidol.edu

Submitted 17 August 2023; Revised 5 September 2023; Editorial Decision 6 September 2023; Accepted 6 September 2023

Plasmodium Knowlesi in HTD (2023)

Case	Chief complaint	Diagnosis	Status
1	39-year-old Burmese man referred to HTD with severe <i>P. vivax</i> malaria	<i>P. Vivax</i> + <i>P.Knowlesi</i> (from Myanmar)	ICU, Recovery
2	19-year-old Thai male referred to HTD with severe <i>P. vivax</i> malaria	<i>P. Vivax</i> + <i>P.Knowlesi</i> (from Keang KraChan, Pethchaburi)	ICU, Recovery

Practical consideration

- Severe *P. vivax* is uncommon >> potential mixed infection or co-infection
- Emerging in *P. knowlesi* in the area through traveler/migration
- Delayed diagnosis can lead to severe manifestation.
- **“Travel History” is important!! in all febrile cases!**



Prevention

- There is vaccine to use in Africa (not available for travelers)
- Malaria chemoprophylaxis
 - Atovaquone-proguanil (Malarone)
 - Doxycycline
 - Mefloquine



Malaria chemoprophylaxis

Malaria risk



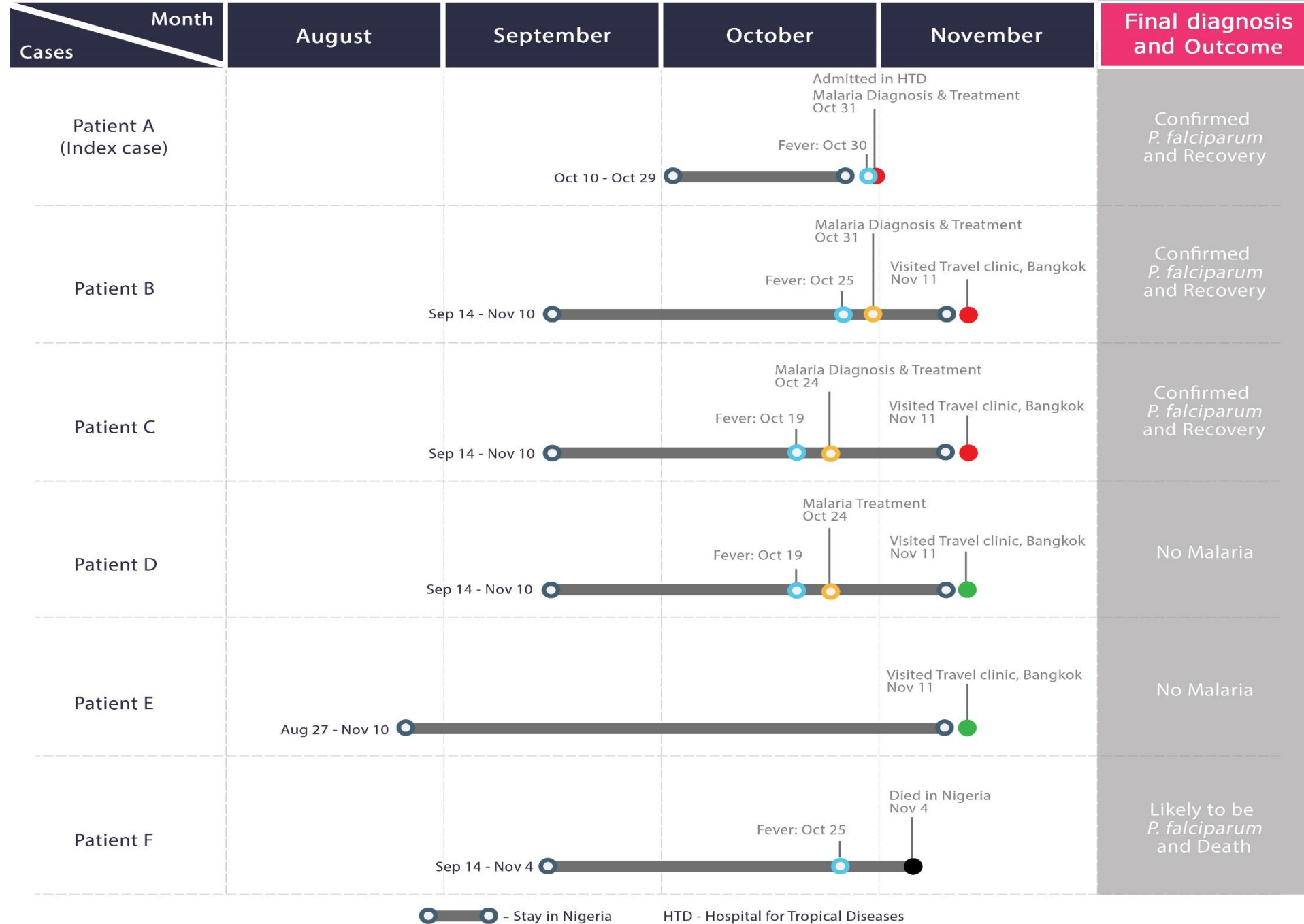
Side effects



DO NOT FOCUS ONLY ON INDIVIDUAL CASE!



- Do not focus only on individual cases but also consider potential disease clusters



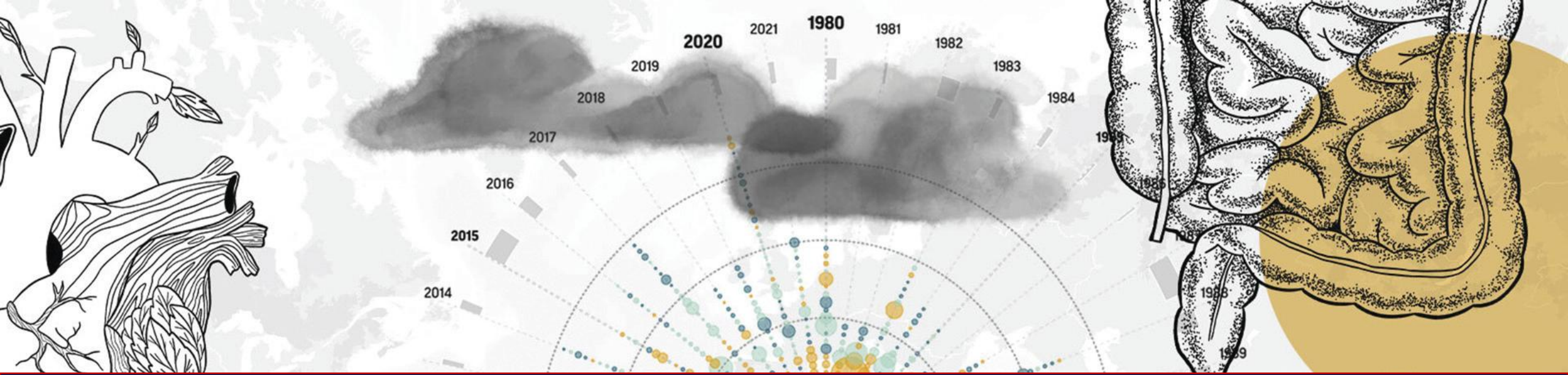
Case Series: Thai workers in Nigeria

	Age	Fever	Event in Nigeria	Seen in HTD	Diagnosis	outcome
A	M, 46y	30 Oct	None	31 Oct	P.f.	recover
B	M, 33	25 Oct	Fever, blood neg	11 NOV	P.f.	

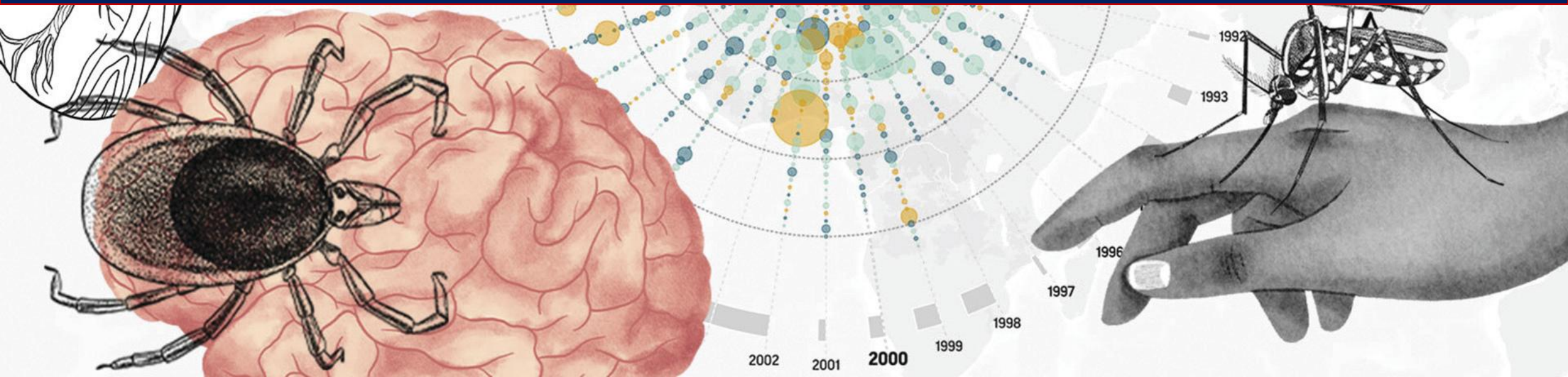
**4/6 Thai workers got malaria in
this trip**

Attack rate = 66.7%

E	F, 45y	24 Oct	No fever, blood neg	11 NOV	All negative	recover
F	M, -	25 Oct	Fever, jaundice, admit 6 days	N/A	Suspected Pf malaria	Died on 4 th Nov



Chikungunya





Chikungunya

- Chikungunya virus is a single-stranded RNA virus that belongs to the family *Togaviridae*, genus *Alphavirus*
- After the 2004–2019 epidemic of chikungunya virus (CHIKV), the largest chikungunya epidemic ever recorded, this disease remains a global problem.
- Three major genotypes of CHIKV are now recognized — the **Asian**, the **West African** and the **Asian and East–Central South African (ECSA)** genotypes
- A new lineage, the **Indian Ocean Lineage (IOL)**, also emerged from the ECSA genotype during the 2004–2019 epidemic



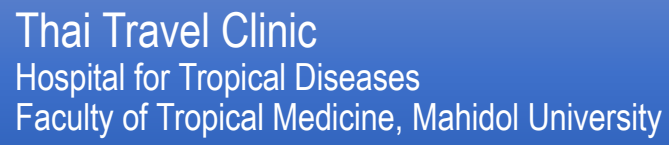
Figure 1: Geographical distribution of CHIKV disease cases as reported to WHO or Publicly shared by Ministries of Health from January to September 2025



The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization, publicly shared data by Ministries of Health
Map Production: WHO Health Emergencies Programme
Map Date: 1 October 2025

0 1,500 3,000 km



The world map illustrates the global distribution of the invasive species, with red dots indicating specific locations and arrows indicating the direction of spread. The map includes labels for various years and year ranges, such as 2010 and 2017, 2007, 2017, 2016, 2014, 2013, 2014-2018, 2014-2017, 2014-2018, 2014-2017, 2014-2018, 2015-2018, 2016, 2010 and 2017, 2007, 2017, 2010 and 2017, 2004-2015, 2006-2007, 2007 and 2010, 2011, 2013 and 2016, 2005-2006, 2011, 2010, 2017, 2013, 2012, 2010, 2010, 2010, 2005-2018, 2005-2019, 2012, 2006, 2008-2009, 2012, 2004, 2006, 2012, 2011-2014, and 2015.



Risk of Chikungunya in travelers

- Risk to travelers is greatest in areas experiencing ongoing chikungunya epidemics
- After the outbreaks in the Americas during 2014–2017, >4,000 chikungunya cases were reported among U.S. travelers
- 13 locally acquired cases were reported in the continental United States
- During 2018–2023, 612 U.S. traveler cases were reported, with noticeably fewer cases during 2020–2021 (COVID-19)

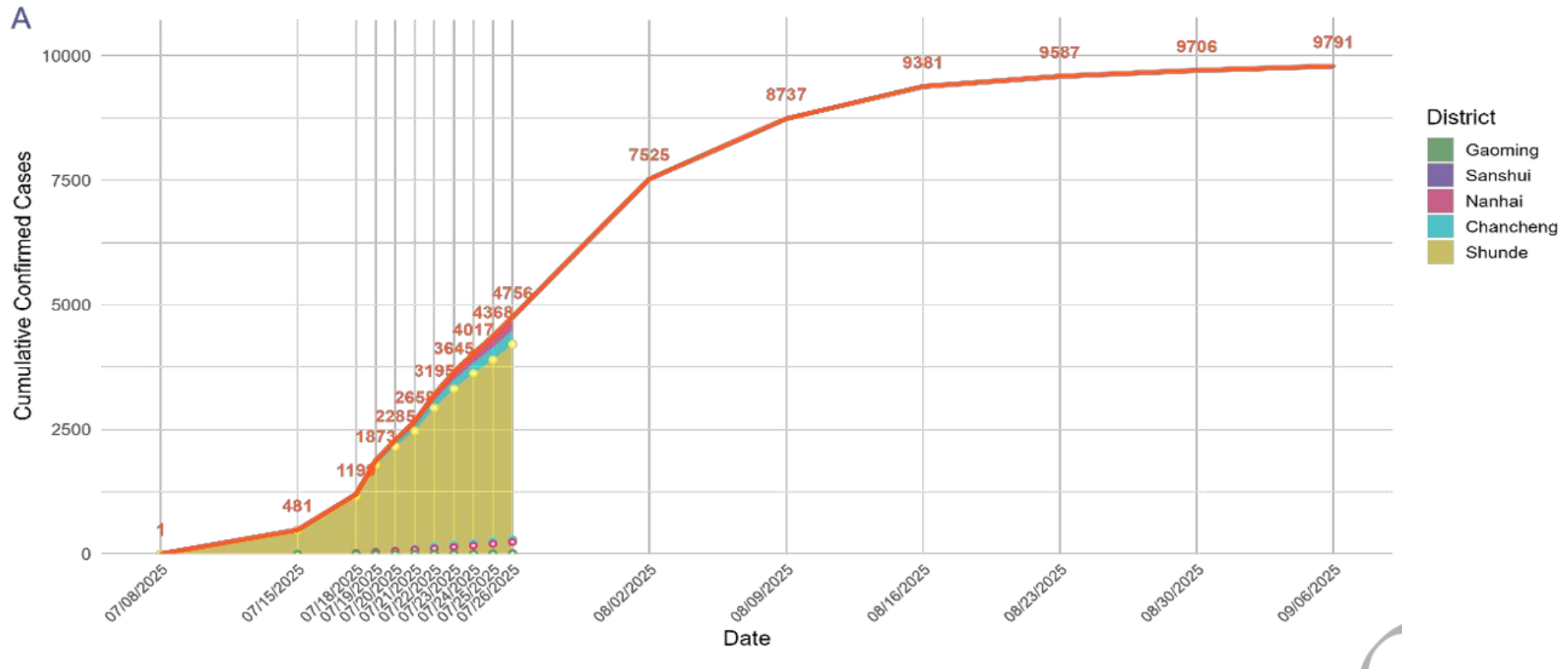


Chikungunya cluster in Guangdong Province 2025

- A detected case on 8 July 2025, has evolved to over 9,000 cases (as of September 6)
- With its climate conducive to **Aedes mosquitoes** and its **high levels of global travel** activities—creates a potential risk area for a chikungunya outbreak
- Whole-genome sequencing of 190 cases revealed that the viral strains exhibited high genomic homology and all belonged to the **Central African clade of the East-Central-South African (ECSA) genotype**
- All cases were mild, no fatal cases reported



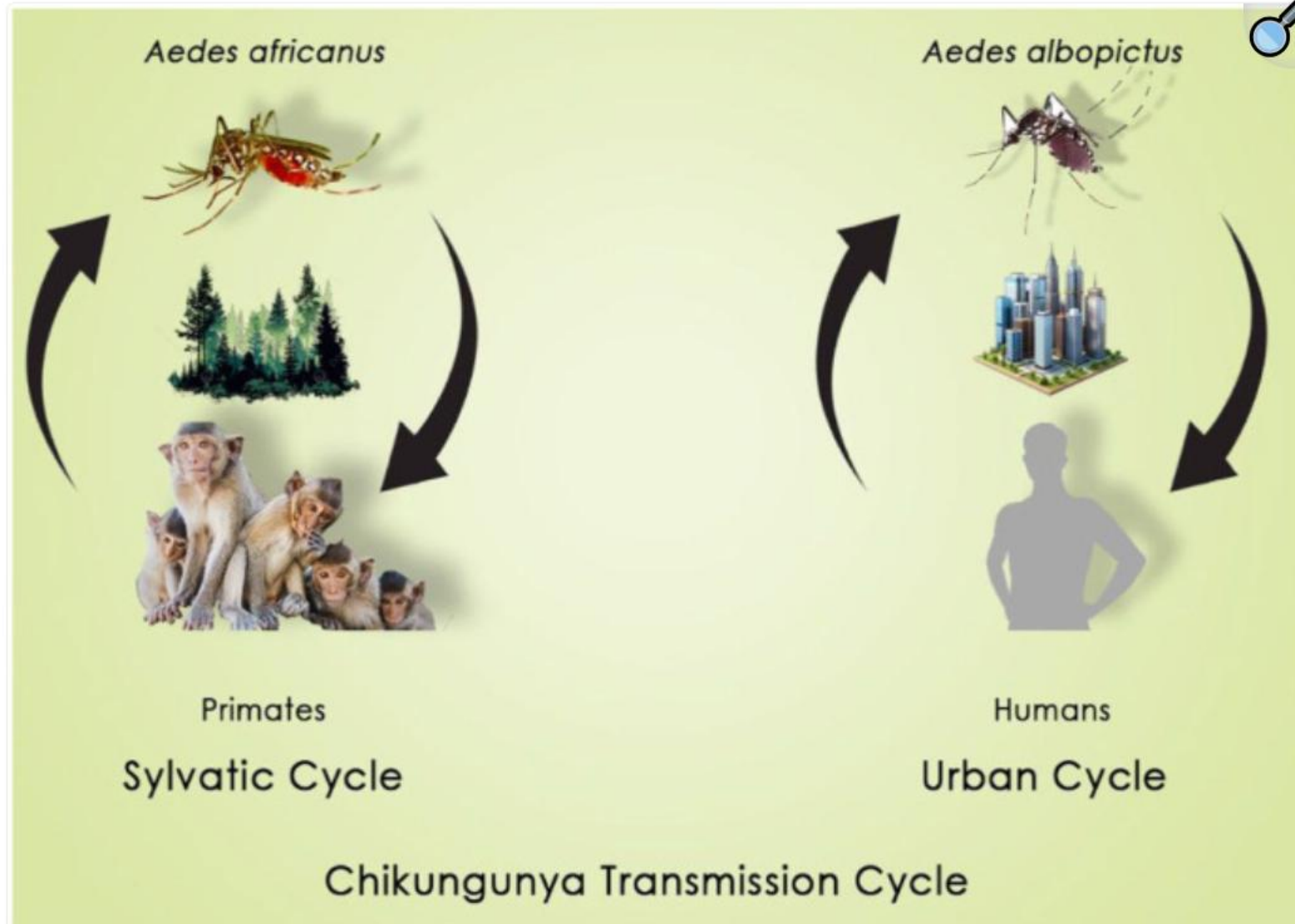
Chikungunya cluster in Guangdong Province 2025





Chikungunya cluster in Guangdong Province 2025

- Travel and trade intensify the risk of CHIKV importation, particularly given Guangdong's status as a major hub for international business, tourism, and labor migration
- The reemergence of chikungunya in southern China reflects broader patterns of arboviral expansion into new territories.
- The convergence of climate change, urbanization, and global mobility continues to push the ecological boundaries of CHIKV.





Clinical manifestation of Chikungunya infection by stage

Stage	Timeframe	Symptoms	Prevalence (%)	Additional notes
Acute	0–14 days	High fever, severe arthralgia, myalgia, rash, headache	88% arthralgia, 90% fever	Severe symptoms may require hospitalization
Subacute	15 days to 90 days (3 months)	Persistent arthralgia, worsening joint symptoms, fatigue	Persistent symptoms in ~30%–40% patients	Symptoms reduce in intensity but persist in some cases
Chronic	>90 days (3 months)	Chronic arthritis, fatigue, depression, neurological disorders, stiffness	Chronic symptoms in 44% patients	May lead to significant long-term disability and reduced quality of life



Table 1 | Typical symptoms of acute chikungunya

Symptoms (duration)	Percentage of patients ^a	Refs
Arthralgia (weeks to months)	80–100	24,118,204–206
Arthritis (weeks to months)	62–100	24,204
Fever (usually lasts 1 week)	80–100	1,118,204
Myalgia (usually lasts ~7–10 days)	10–85	1,24,118,205,206
Headache	30–90	24,118,205,206
Rash (usually lasts ~1 week)	36–88	1,24,118,204,205,207
Fatigue	43–67	118,207
Diarrhoea	25	24,205
Oedema	22–39	24,206

^aPercentages of patients with the indicated symptoms, with the ranges encompassing all referenced studies.

Table 2 | Atypical symptoms of acute chikungunya

Systems/organs affected	Percentage of hospitalized patients ¹⁰	Manifestation examples	Refs
Neurological	40	Encephalitis Meningoencephalitis Guillain–Barre syndrome	38–41,43
Cardiovascular	27	Hypotension Myocarditis Arrhythmias	38–41
Skin	10	Hyperpigmentation Bullous dermatosis Erythema	38–41
Renal	26	Albuminuria Haematuria Nephritis	39,40,45
Respiratory	14–26	Dyspnoea Respiratory failure Pneumonia	38,39,41
Vascular	10	Haemorrhagic signs Bleeding gums Melena	39,41,205,208,209
Ocular	Less common than other atypical symptoms	Conjunctivitis Photophobia Retinitis	39,41,210,211
Liver	Less common than other atypical symptoms	Hepatitis Hepatomegaly Altered function	38,40,41

Atypical acute manifestations can accompany the typical acute symptoms (TABLE 1). Atypical manifestations are grouped by the systems/organs affected, with some examples of manifestations provided; these are neither complete nor ranked and the reader is directed to the accompanying references for a full description of manifestations.

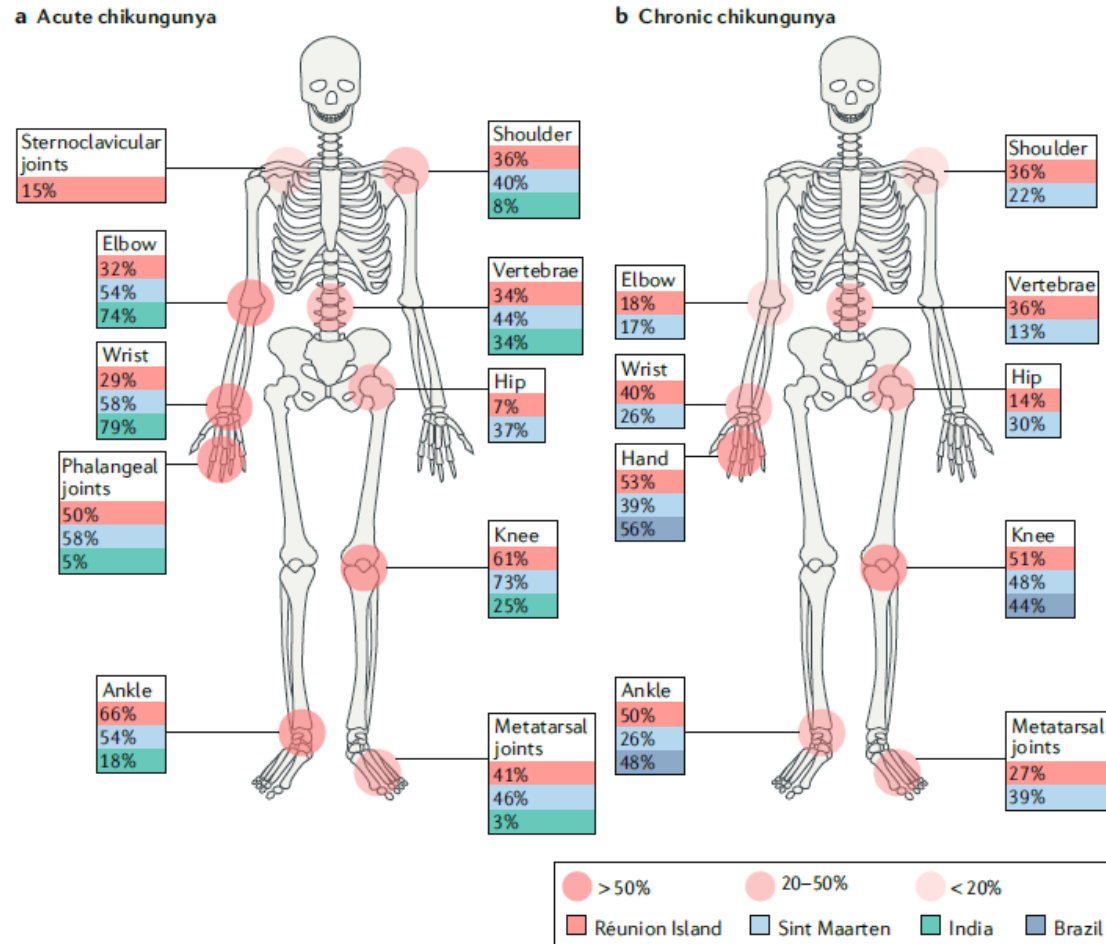


Fig. 2 | Joints affected by chikungunya arthralgia. a | Joints with arthralgia at or near the time of disease onset, indicating the range of percentages of patients reporting arthralgia in each indicated joint or group of joints in previous studies of patients with acute chikungunya on Réunion Island¹⁹⁹, on Sint Maarten in the Caribbean²⁰⁰ or in India²⁰¹. b | Joints with arthralgia in patients with chronic chikungunya, based on data from patients with chronic chikungunya on Réunion Island¹²⁰², on Sint Maarten in the Caribbean²⁰⁰ or in Brazil²⁰³. Assessment methodologies were not standardized in these studies, and so it is difficult to attribute any differences across these studies to CHIKV genotypes or specific populations.



Clinical comparison between Chikungunya, Dengue, and Zika

Feature	Chikungunya	Dengue	Zika
Fever	+++	+++	++
Arthralgia	+++	+	++
Headache	++	++	+
Skin rash	++	+	+++
Myalgia	+	++	+
Conjunctivitis	—	—	++
Shock	—	+	—
Hemorrhage	—	++	—



Chikungunya





Thai Travel Clinic
Hospital for Tropical Diseases
Faculty of Tropical Medicine, Mahidol University





Thai Travel Clinic
Hospital for Tropical Diseases
Faculty of Tropical Medicine, Mahidol University



Arthritis in Chikungunya infection



Cutaneous manifestations during chikungunya fever

- (A) Milians ear sign.
- (B) Maculopapular rash.
- (C) Scar phenomenon.



Other Cutaneous Involvement Associated with CHIKV

A) MP rash; B) Convalescence rash; C) Urticaria; D) CHIK sign; E) Millian's ear sign, F) Erythema of the nose; G) Erythema of the hand H) Panniculitis



Severe chikungunya is relatively rare

Box 2 | Severe symptoms of acute chikungunya

Severe symptoms of acute chikungunya (listed below) are defined as manifestations that include dysfunctions of at least one organ or system that threatens life and requires hospitalization. The term “failure” reflects a spectrum that includes non-lethal manifestations with recovery.

- Cardiac failure^{17,38,41,42}
- Multiple organ failure^{17,38}
- Viral sepsis and/or septic shock⁴²
- Renal failure^{10,17,38,42,45}
- Liver failure^{10,17,38,42}
- Respiratory failure^{10,17,38,42}
- Encephalitis or meningoencephalitis^{17,38,42,43}
- Bullous dermatosis^{17,38}



International Society of Travel Medicine
Promoting healthy travel worldwide
Established 1991

Journal of Travel Medicine, 2019, 1–2
doi: 10.1093/jtm/taz033
Clinical Pearls

Clinical Pearls

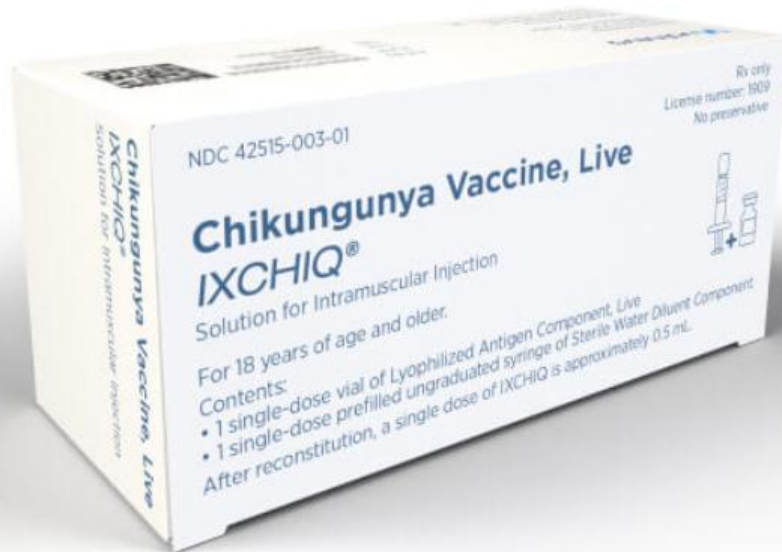
Severe chikungunya requiring intensive care in two travellers returning to the UK

Claire Calderwood, MRCP¹, Sanjay Bhagani, FRCP¹, Ian Cropley, FRCP¹, and Padmasayee Papineni, MRCP^{2*}

¹Department of Infection, Royal Free London NHS Foundation Trust, London, UK and ²Department of Infectious Diseases and Tropical Medicine, Ealing Hospital, London North West University Healthcare NHS Trust, London, UK



Chikungunya Vaccine



IXCHIQ (Valneva VLA 1553)

- live attenuated vaccine
- 61 aa deletion: NS3
- Excellent serologic response
- immunity is maintained for at least 2 years after vaccination
- **Prolonged (>30 days) chikungunya-like symptoms** in a surprising % of vaccines buried in Supplemental data



Chikungunya Vaccine

**FDA and CDC Recommend Pause in Use of
Ixchiq (Chikungunya Vaccine, Live) in
Individuals 60 Years of Age and Older While
Postmarketing Safety Reports are
Investigated**

May 9, 2025

Safety Communication

IXCHIQ (Valneva VLA 1553)

- **17 serious adverse events**
- **2 death** in 62, 89 years old (encephalitis)
- Some recipients had prolonged
chikungunya-like adverse reactions that
lasted for at least 30 days.



Chikungunya Vaccine



JOURNAL ARTICLE ACCEPTED MANUSCRIPT

A new non-live chikungunya vaccine for travellers

David O Freedman, MD ✉

Journal of Travel Medicine, taaf039, <https://doi.org/10.1093/jtm/taaf039>

Published: 13 May 2025 **Article history** ▼

VIMKUNYA

- Virus-like particle vaccine
- Based on 3 non-structural proteins
- Single dose
- **Day 22 seroresponse rate: 98%** (adolescents/younger adults) vs. **87%** (older adults)
- **6 months** seroresponse rate: **85%** (adolescents/younger adults) vs. **76%** (older adults)
- US FDA and EMA approved in February 2025
- Recommended for travellers >12 years of age



Take Home Message

- **Fever is common in returned travelers**
- **Malaria is the common of cause of febrile travelers returning from Africa and can be further prevented through the appropriate use of chemoprophylaxis.**
- **The risk of mosquito-borne illnesses can be reduced by behavioral changes and use of insect repellent, screens, netting, and insecticide-impregnated clothing.**
- **Travel History and travel exposure is a key to diagnosis**

THANK YOU
多謝你

Contact: wasin.mat@mahidol.ac.th

