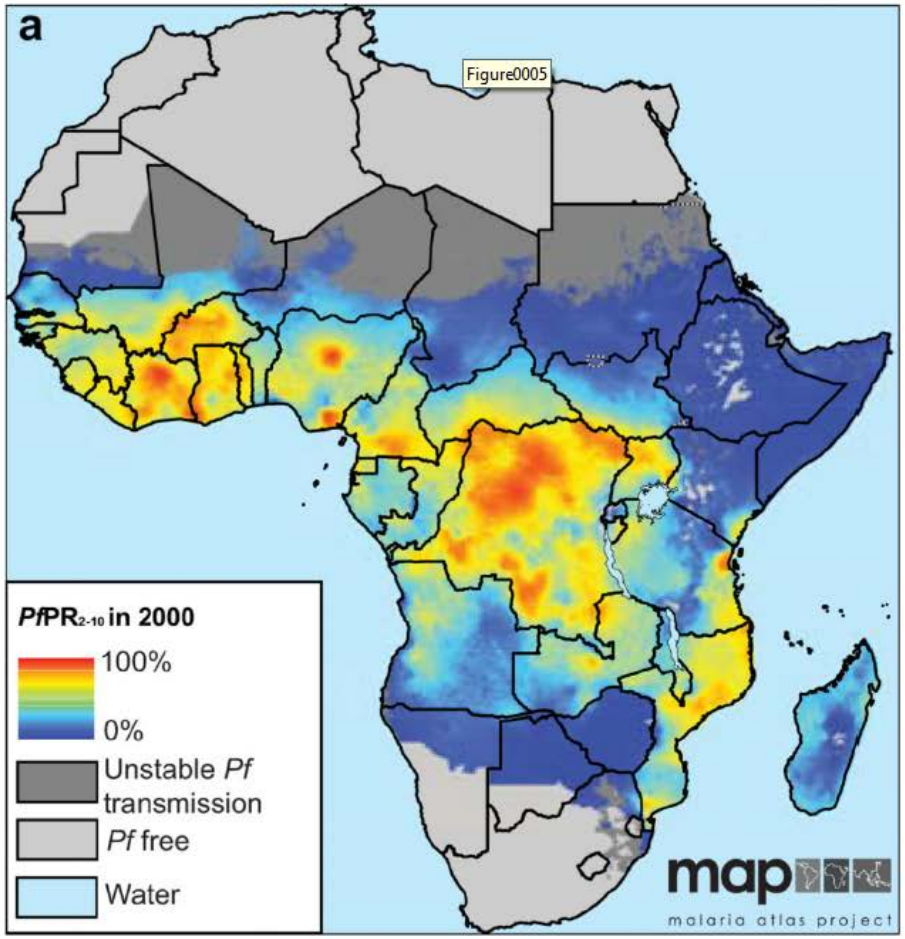
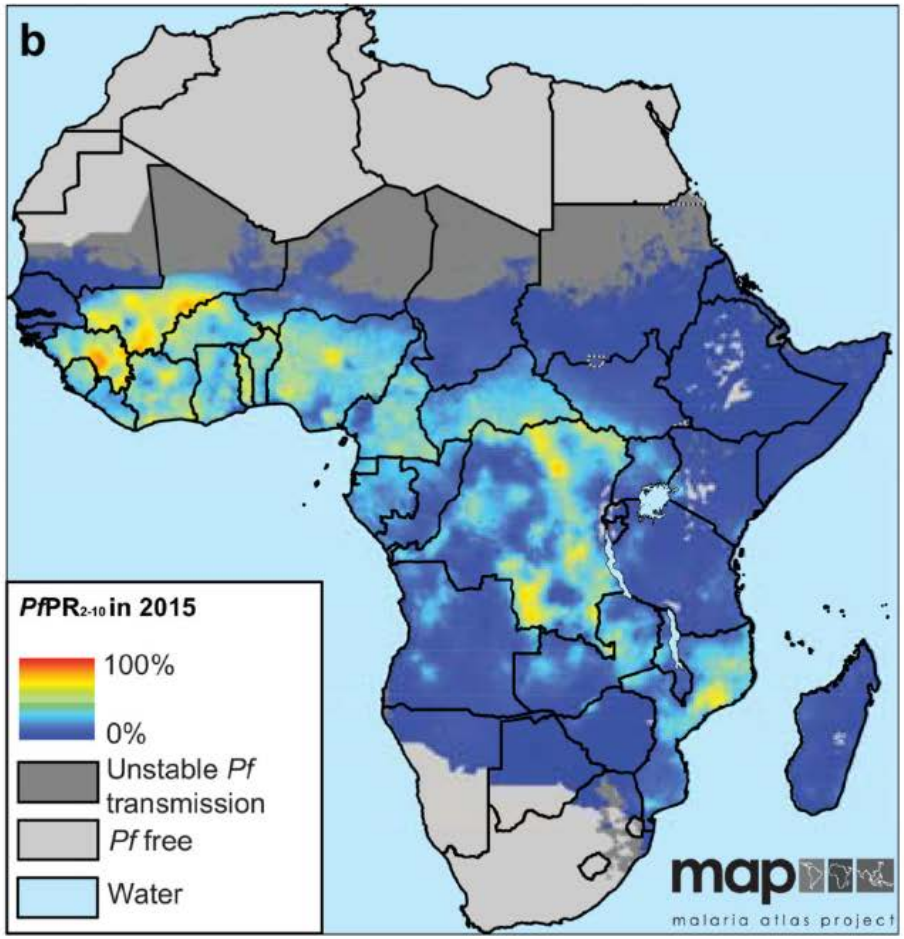
Changing malaria risk for travellers

Swiss TPH Winter Symposium 2016
Christoph Hatz, Swiss TPH

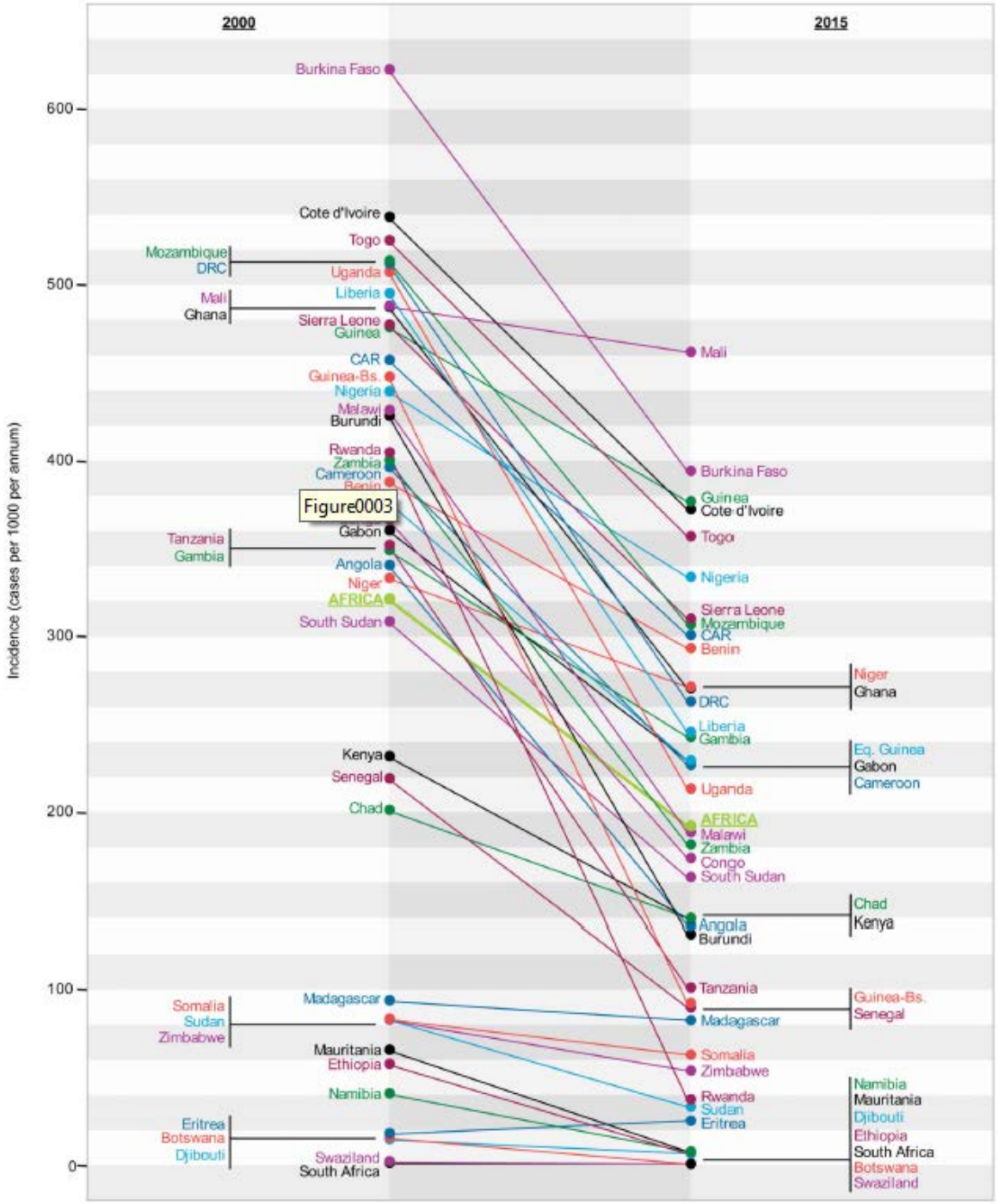
Changes in infection prevalence 2000-2015

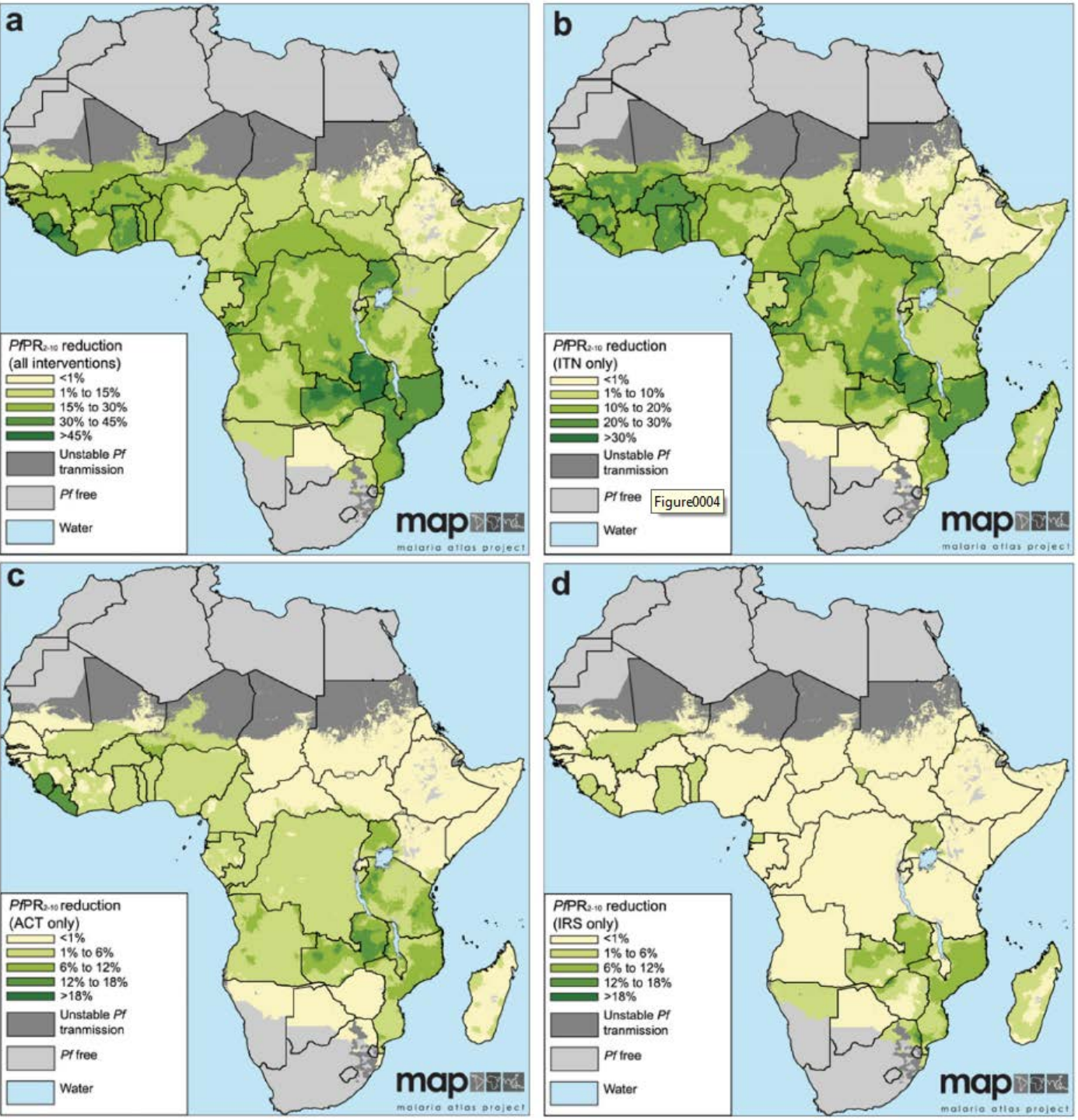




Malaria mortality: 25% Global reduction 33% reduction in WHO Africa Region over the last 10 years: > 1 Million lives saved

Changing incidence rate by country 2000-2015





Decline in infection prevalence attributable to main malaria control interventions (2000-2015)

Malaria
Urban-Periurban-Rural

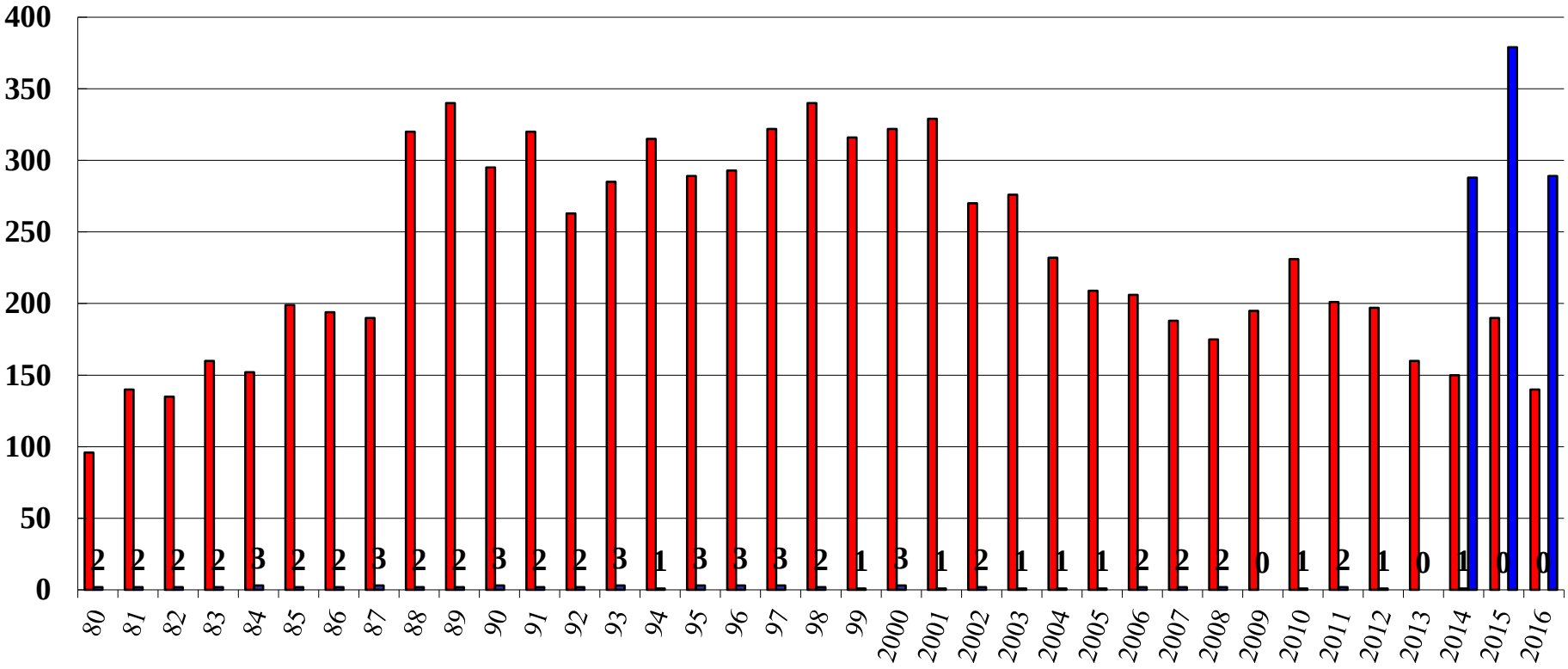
Africa	18.8	63.9	126.3 (EIR)
Ouaga	24.1	38.6	68.7 (PfPR)

But: Libreville: 80 infective bites/person/year

Factors: Location (altitude; proximity to sea, river, lake or floodplain, ponds, **swamps**); climate, land use (**urban agriculture**), human movement patterns, socioeconomic factors (poverty!); waste management; (clean) vector breeding sites; vectors; local malaria intervention programmes. Urban dwellers to rural areas!

Carme, 1994; Keiser, 2004; Hay, 2005; ***De Silva, 2012;*** *Kigozi, 2015; Bouyou-Akotet, 2016*

Malaria cases in Switzerland (FOPH)



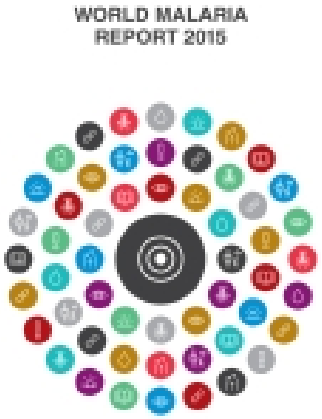
Number of reported cases / 0-3 deaths per year

Overall number of cases (travellers) / number of cases including refugees (2014-16; mainly from the Horn of Africa)

Trends in **imported malaria** in industrialized countries (estimated 15‘000-30‘000 cases/annum)

Country	Residents	*Immigrants*	*Schlagenhauf, 2015*
Spain	+	+ + +	*Lopez-Velez, 1999, 2010, 2015*
Italy	+	+ + +	*Matteeli, 1995, Castelli, 1999. Calleri, 2013*
Switzerland	+	+ + +	*Antonini, 1996; FOPH, 2015, Swiss TPH 2016*
Germany	+ +	+ + +	*Schönberg, 1998, RKI 2015*
Holland	+	+ + +	*Wettsteyn, 1997, Baas, 2006; Vliegenthart 2013*
France	+	+ + +	*Parola, 2006*
United Kingdom	+	+ + +	*Behrens, 2006, HPR 2010, 2015*
USA/Canada	+	+ + +	*Skarbinski, 2006, MMWR 2010; Boggild, 2014*
Norway	+	+ +	*Jensenius, 1999*
New Zealand	+ +	+	*Shew, 1995*

Background Information for recommendations

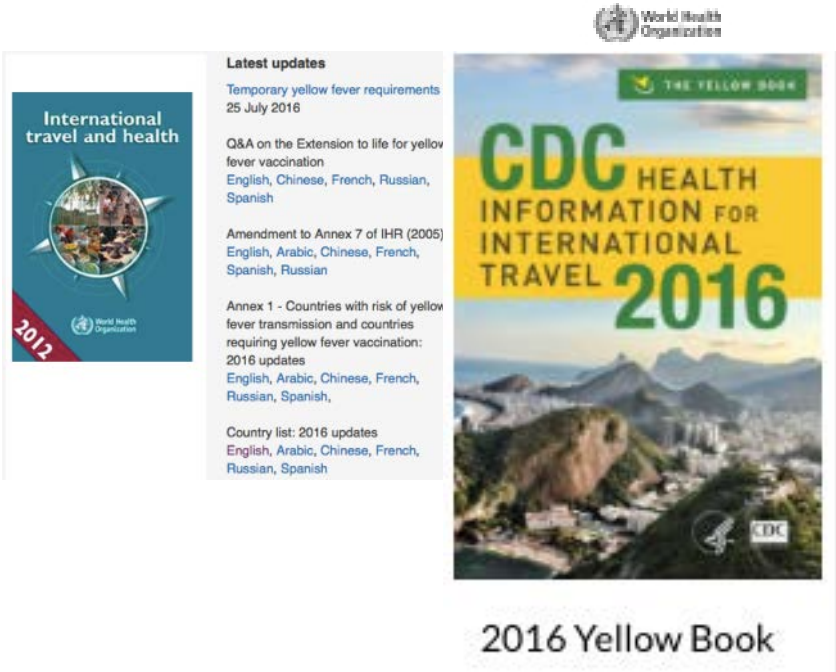


- **World malaria report**
- WHO, ITH malaria recommendations
- CDC Yellow Book
- ECDC
- PAHO

- Malaria cases by country
  - Ministry of Health by countries
- Malaria in **travellers**
  - National statistics

- Tourist data
  - WTO
    - Information from Expert Committee for Travel Medicine

- Private sector (commercial companies)



2016 Yellow Book

Criteria for strategic choice

1. Evidence- and travel-related-based information: few data avalable
2. WHO data on endemicity
3. Mixed criteria: data on travellers plus annual parasite index (API)
3. «Any place where malaria transmission occurs» (US legal practice)

Behrens, 2008, 2010; CDC, 2013; Calleri, 2014; Caumes, 2014, WHO, 2015; Pechel, 2015

Definitions for malaria prevention (Switzerland)

- Minimal risk (➔ only mosquito bite avoidance): in the **last 5 years:**
  - **Less than 1 documented case in travellers or 1 case per 100' 000 travellers**
  - No local or only few isolated malaria cases in the indigenous population, or
  - API <= 1/1000 indigenous people

- Low risk (➔ Stand by emergency treatment = SBET): **per year:**
  - **1-10 documented cases per 100 000 travellers**
  - <= 10-(50?) locally documented cases in indigenous population or
  - API 2-10 (50?) / 1000 indigenous population

- High risk (➔ chemoprophylaxis = P): **per year**:
  - **>10 documented cases per 100 000 travellers**
  - > 10 (>50?) locally documented cases in indigenous population or
  - API >10 (>50?)/ 1000 indigenous population

Source: Hatz et al., 2016

Malaria prevention strategies

1. **Mosquito bite avoidance**
2. Presumptive treatment in case of fever if no medical care can be reached within 24 hours: **Emergency or Stand-by self-treatment**
3. Continuous drug intake to prevent disease development: **Chemoprophylaxis** (=suppression)

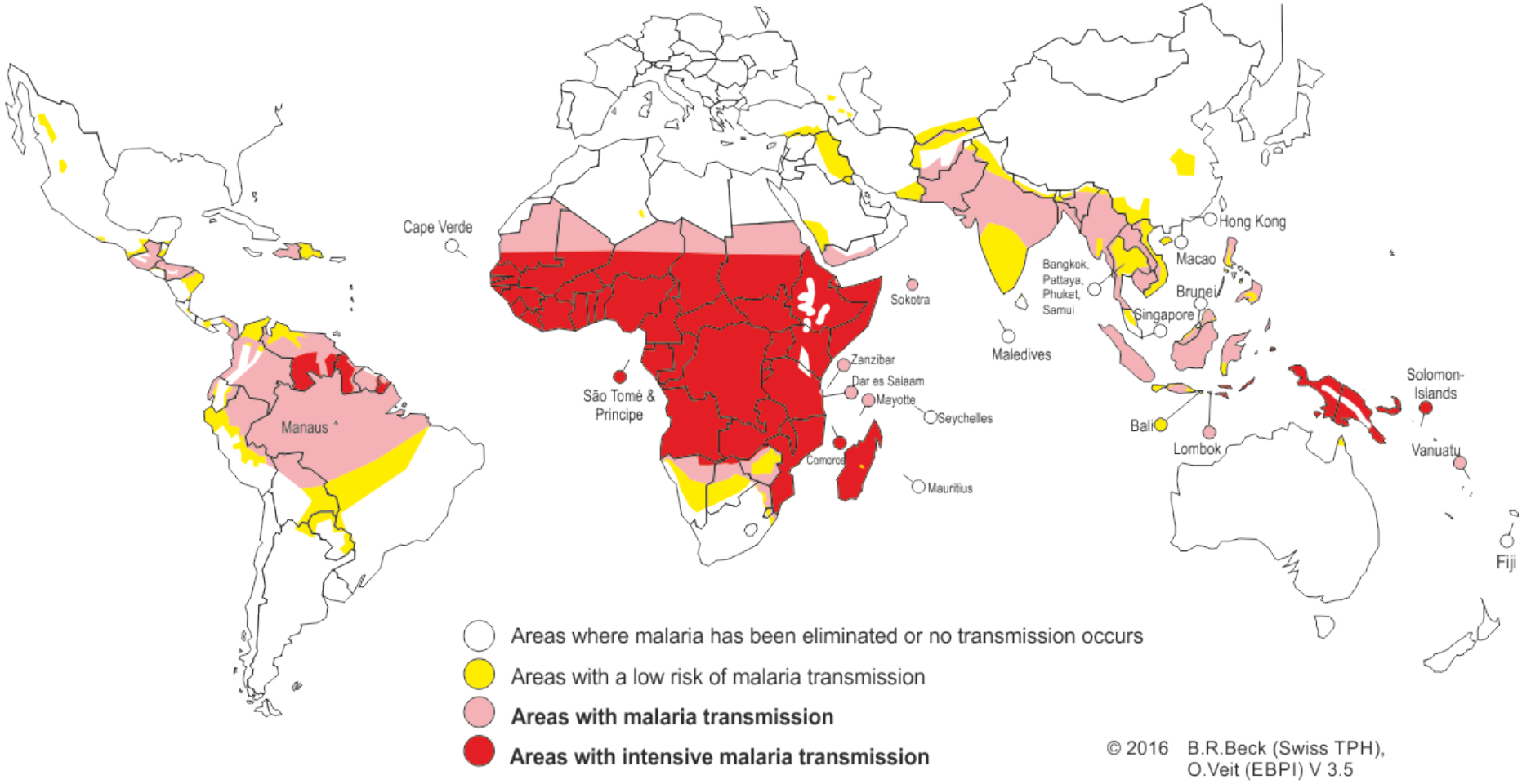
Option: Strategies 2 and 3 with Rapid Diagnostic Tests

Awareness of malaria is key

Reasons for **S**tand-**b**y **E**mergency self-**T**reatment (SBET)

- Travelling over long periods in aread where no medical help can be reached in case of fever
- Avoidance of receiving fake drugs abroad = readily available safe drug
- Travelling in areas with (minimal), low or moderate transmission risk (benefit-risk assessment of chemoprophylaxis)
- Raised malaria awareness

Malaria 2016



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Malaria Prophylaxis 2016

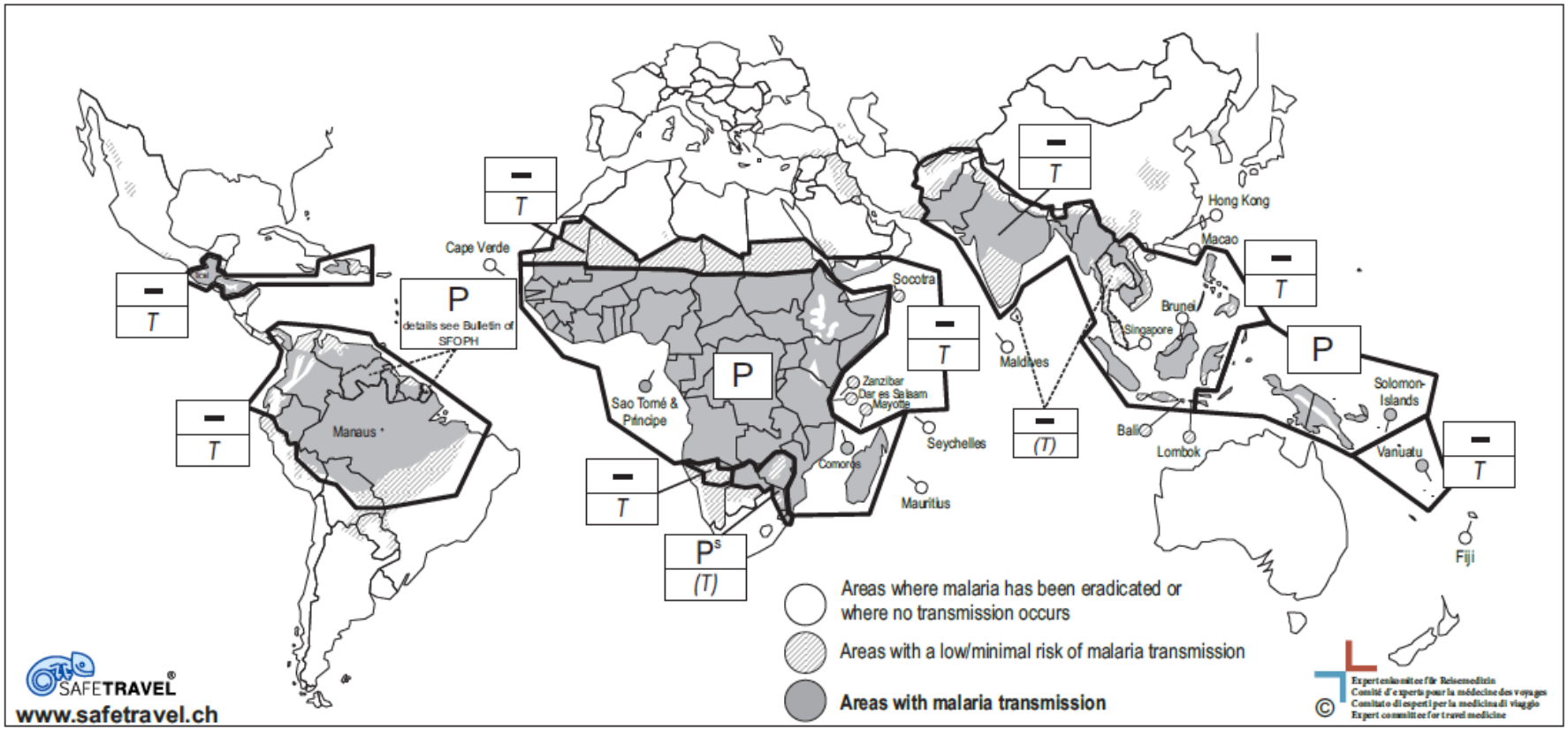
Recommendations by the expert committee for travel medicine (ECTM / Switzerland).

1.) Protection against mosquito bites is recommended in all endemic regions, including areas where the risk is considered minimal*.

2.) Chemoprophylaxis and/or emergency self-treatment are prescribed based on the travel destination*.

* a detailed list of countries is regularly published in the Bulletin of the Swiss Federal Office of Public Health (SFOPH) in French and German [http://www.bag.admin.ch].

P	Atovaquone/proguanil **APP**, Mefloquine **MP** or doxycycline **DP** for chemoprophylaxis
P^s (T)	Chemoprophylaxis **(seasonal)** recommended: atovaquone/proguanil **APP**, Mefloquine **MP** or doxycycline **DP** *Carry **standby emergency self-treatment**: artemether/Lumefantrin **ALT** or atovaquone/proguanil **APT** in special situations (See Bulletin of the SFOPH)*
– T	**No chemoprophylaxis** is recommended. Carry artemether/lumefantrin **ALT** or atovaquone/proguanil **APT** for standby emergency self-treatment
– (T)	**No chemoprophylaxis** is recommended. *Carry **standby emergency self-treatment**: artemether/Lumefantrin **ALT** or atovaquone/proguanil **APT** in special situations (See Bulletin of the SFOPH)*



Adapted from: WHO International Travel and Health 2015 & World Malaria Report 2015

Vers. 3.51 / 2016-02 *Swiss TPH, Basel/ B.R.Beck; EBPI, UZH/ O. Veit*

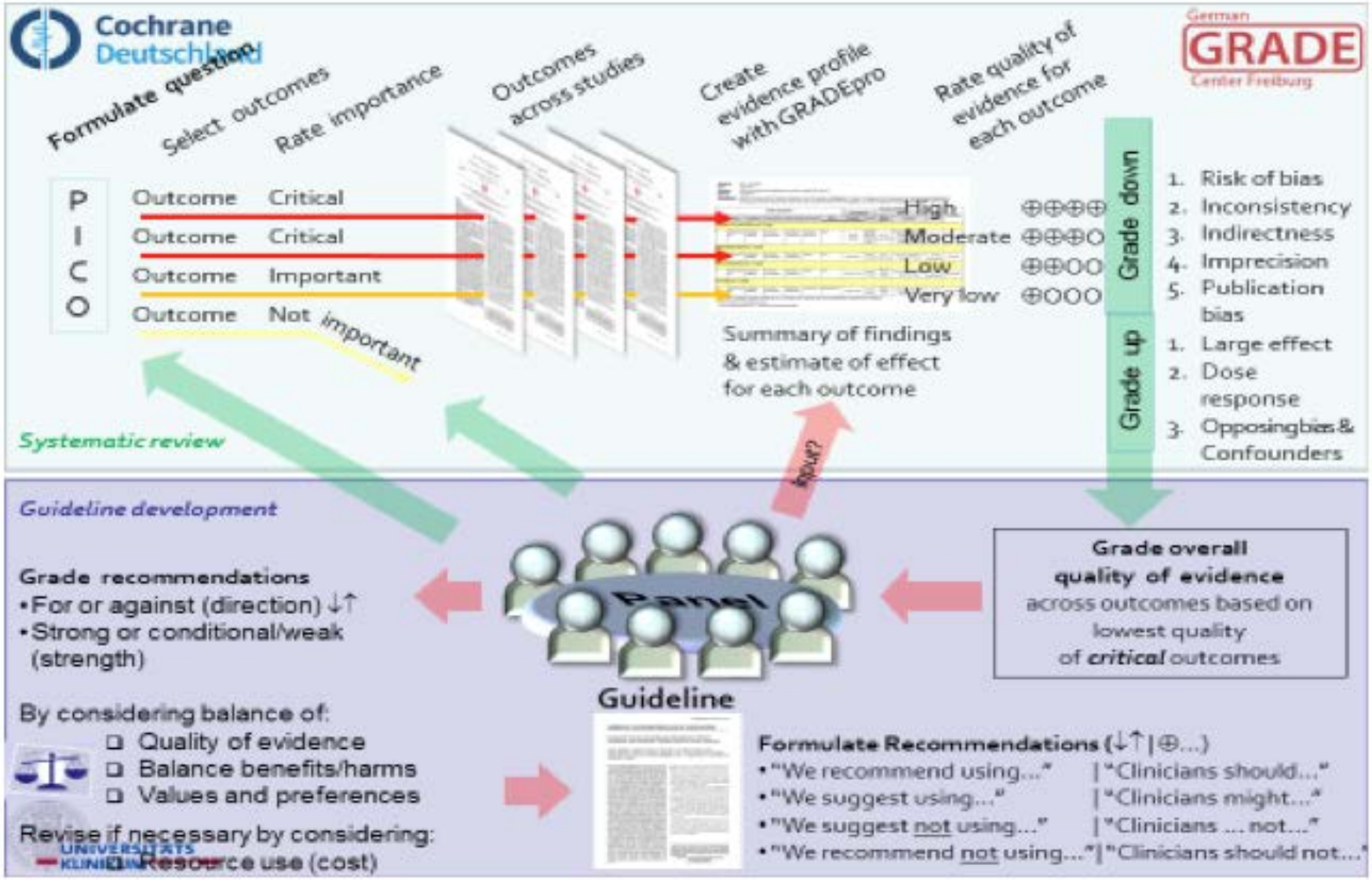
Factors of uncertainty

Do travellers go to the risk areas in countries with high, moderate or low transmission risk? What are the exact protection conditions apart from mosquito repellents and chemoprophylaxis?

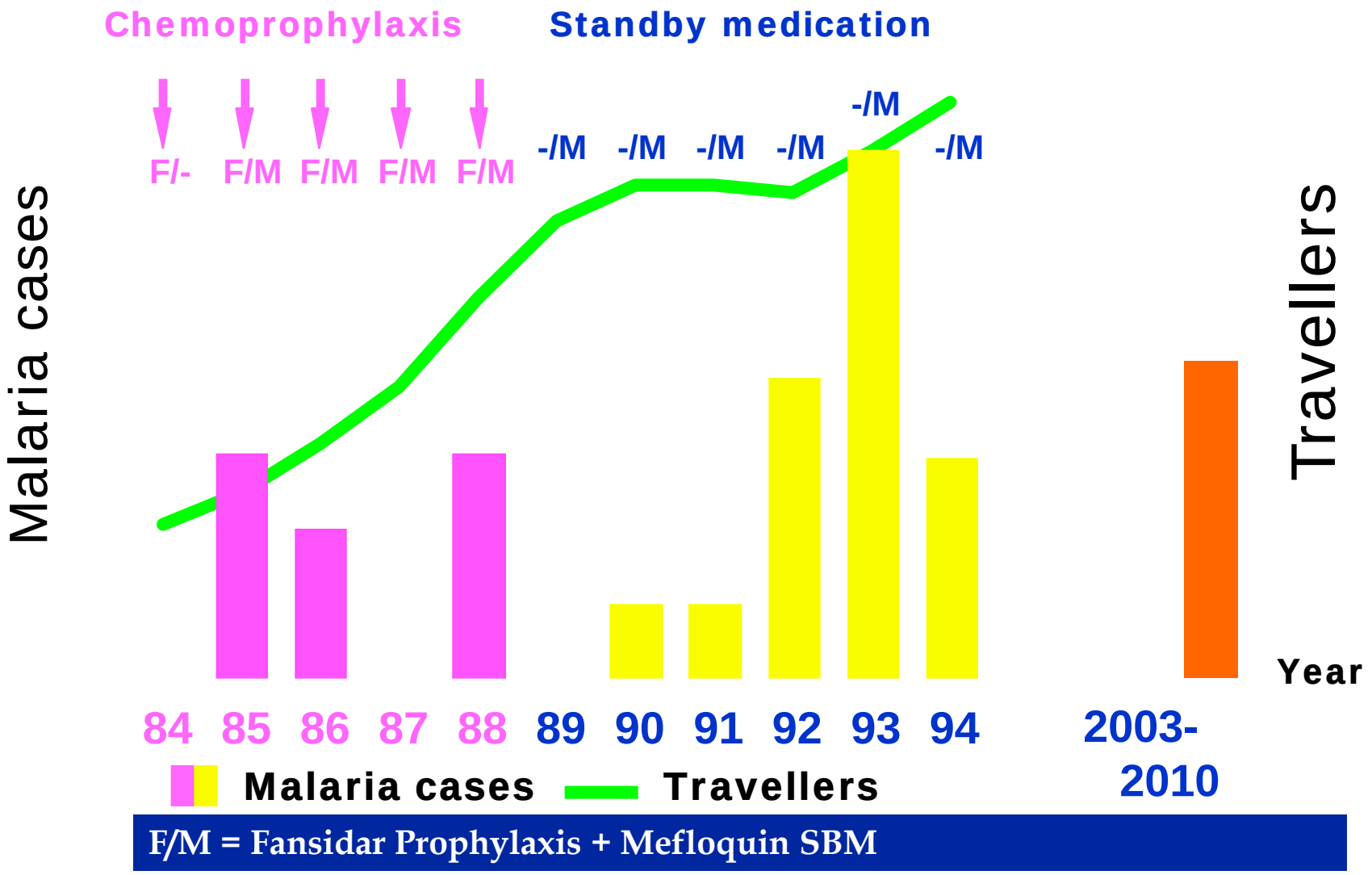
- Seasonality (fluctuation) of malaria transmission.
- Individual factors of travellers.
- ‘Semi-Immunity of ‘Visiting Friends and Relatives’ with immunological background of malaria exposure during childhood

GRADE: PICO-questions on Population, Intervention, Comparison

Figure 1: Summary of the GRADE Framework for developing recommendations



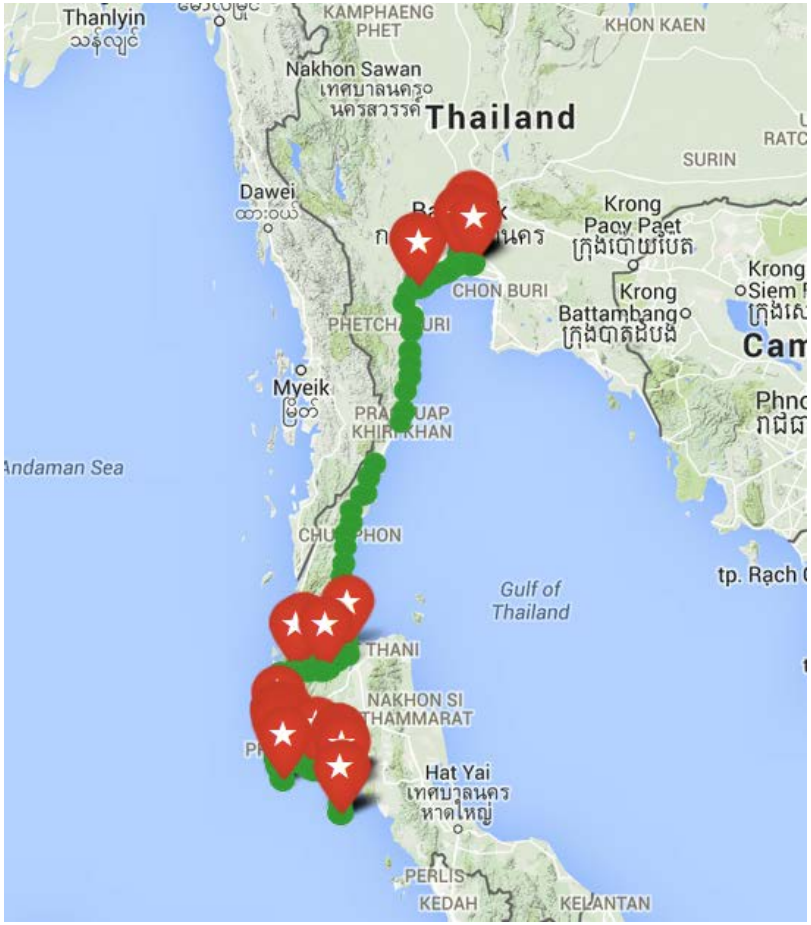
Imported malaria cases in Switzerland from Thailand

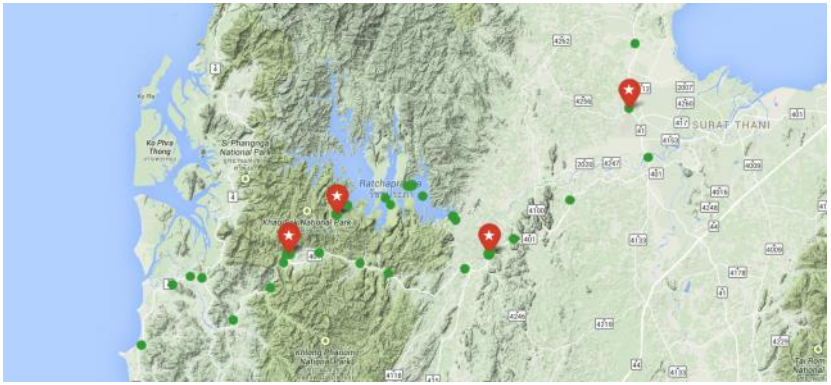


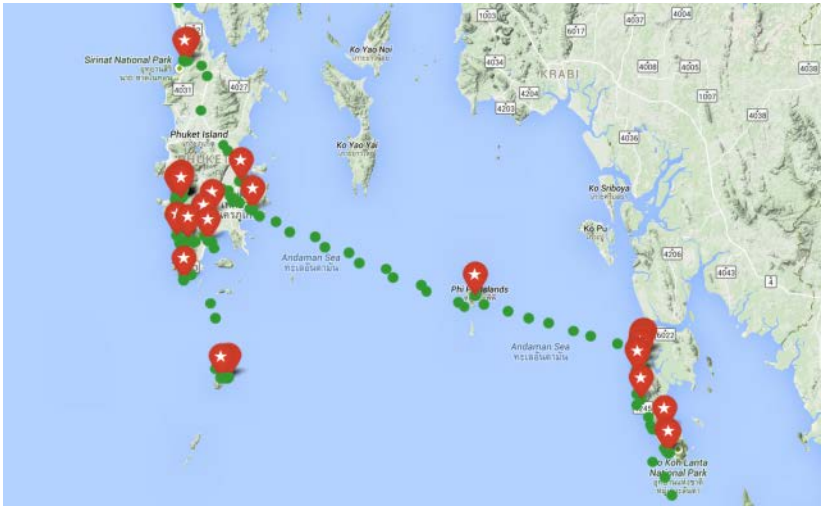
Imported malaria cases from SE Asia in 11 European countries and the US

Land	Malaria cases	Total trips	Cases / trips
Thailand	39	61‘672‘893	1:1‘581‘356
Malaysia	4	103‘283‘549	1:25‘820‘887
Kambodscha	18	9‘018‘465	1:501‘026
Burma	12	933‘147	1:77‘762
Laos	3	4‘542‘684	1:1‘514‘228
Indonesien	61	25‘167‘397	1:412‘580
Vietnam	7	20‘834‘023	1:2‘976‘289
Korea	41	36‘087‘802	1:880‘190

Travellers' itineraries: Using data collected by apps to assess exposure risks





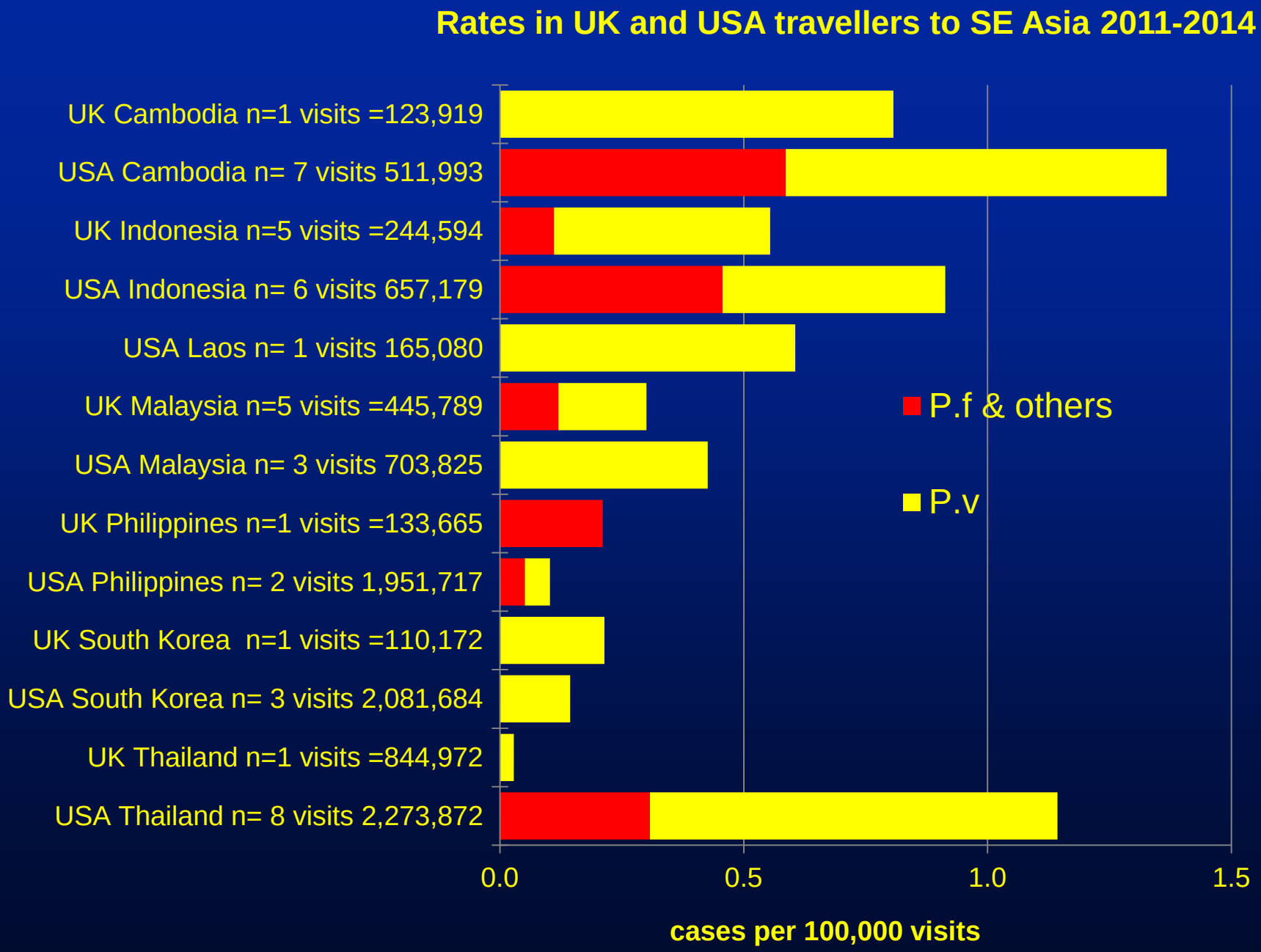


Farnham, 2016

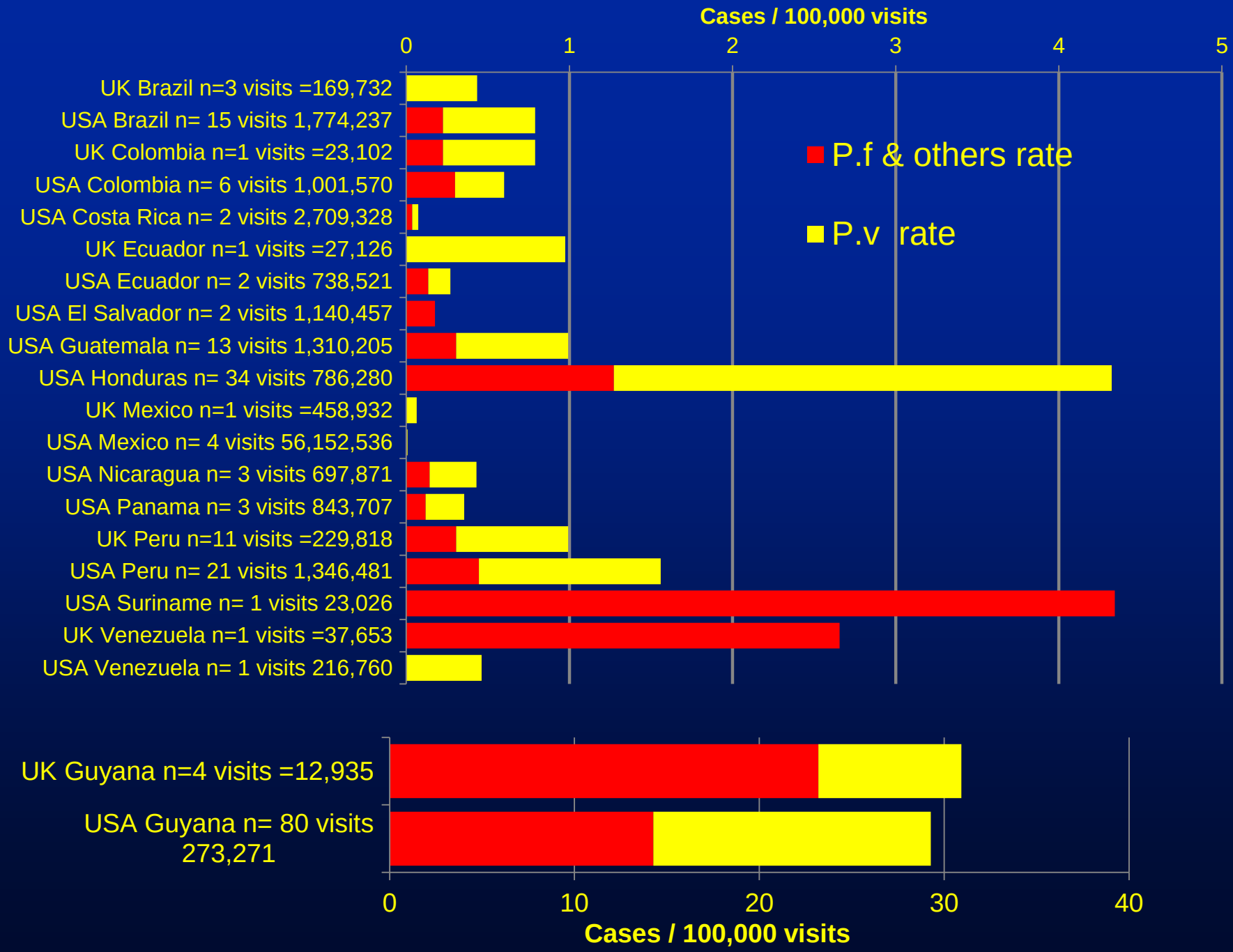
Just for the fun of it:
… a few calculations..

- Letality of malaria: ~1%
- Risk of malaria in a European in **Thailand**: 1:1,5 mio
- Risk of malaria death in Thailand: 1:150 mio
- With >150‘000 yearly Swiss travellers, this indicates the risk of one death in 1000 years

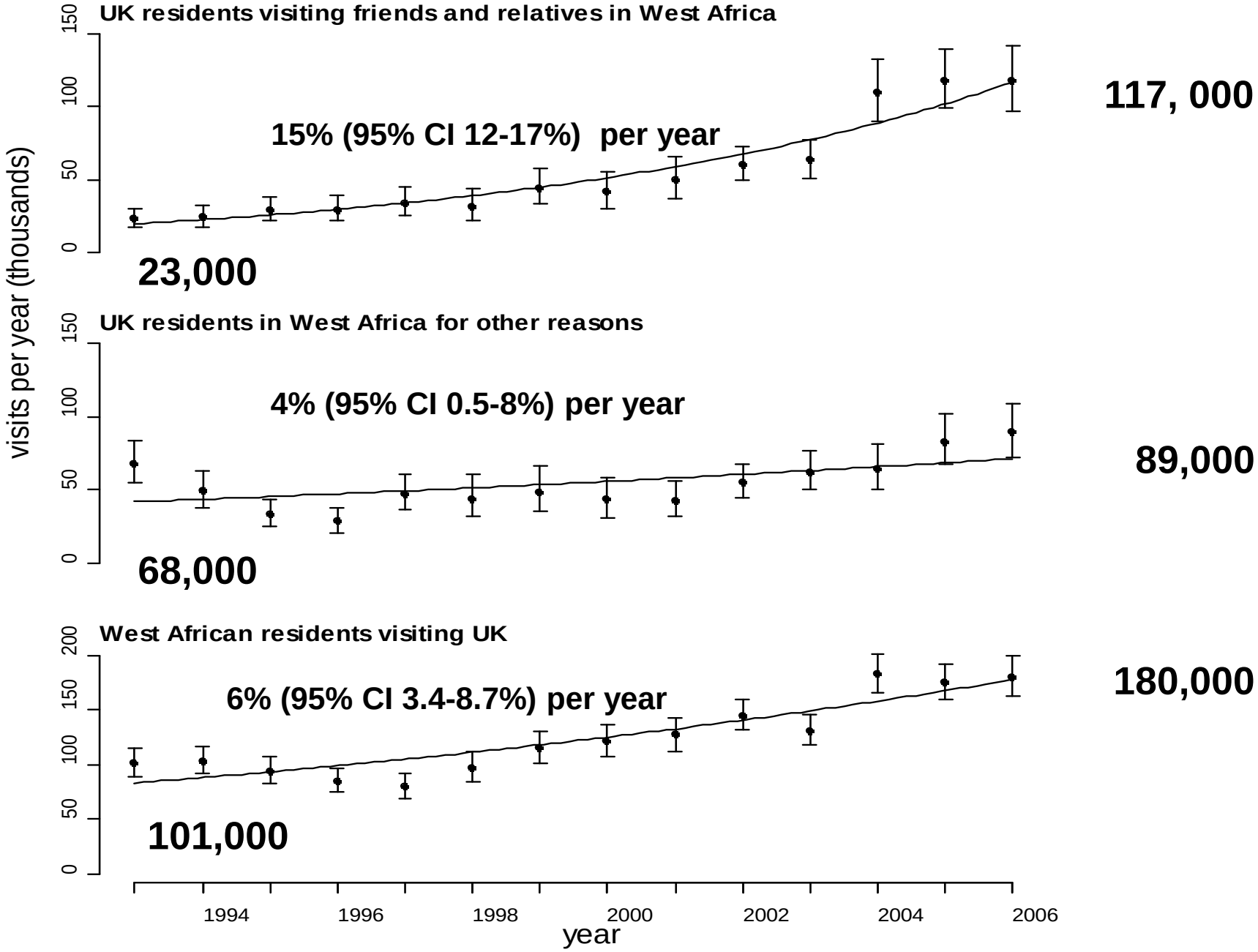
Incidence of malaria in South East Asia



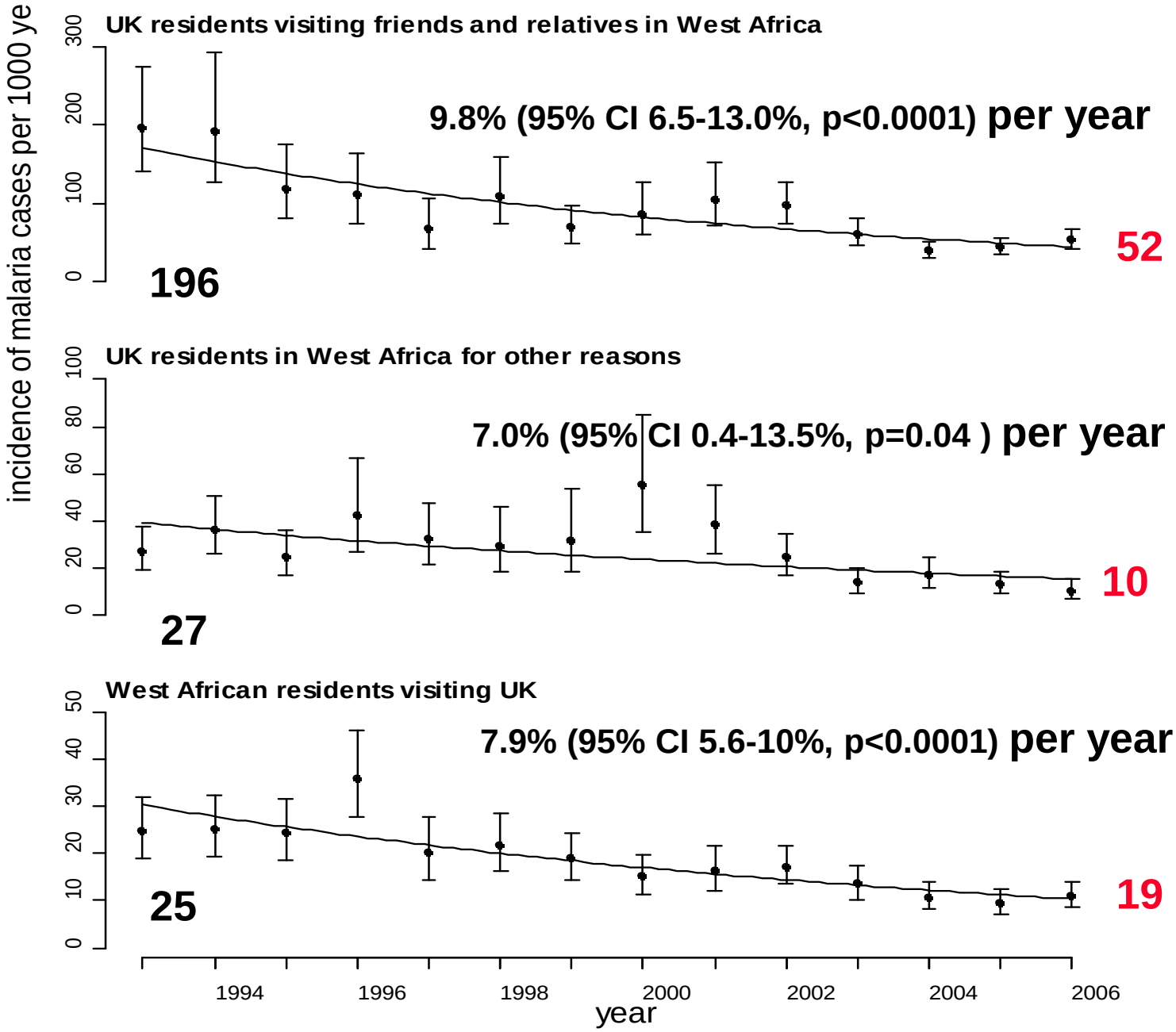
Incidence of malaria in South America



Travel in UK residents and visitors to and from West Africa 1993-2006



Malaria incidence 1993-2006 in residents and visitors to and from West Africa



Chemoprophylaxis in areas with high prevalence of *P. vivax*-malaria

- The first attack will be suppressed
- Will the second attack be missed before it appears (much) later?
- General consensus: chemopropylaxis not useful for suppressing P. vivax infections unless we will have drugs to eradicate liver stages.

Summary

- Malaria exposure risk awareness must be kept high among travellers to avoid deaths.
- Stress mosquito bite avoidance.
- Travellers' malaria measured by imported rates is an objective measure of generic risk
- Exclusive use of local and/or geographical perceived risk leads to subjective and conflicting estimates
- For the time being, pragmatic assessment of available data and avoidance tools must be used for making recommendations.

Thanks to Olivia Veit, Bernhard Beck, Christian Lengeler, Anne McCarthy, Ron Behrens, the ECTM and to ..

... you for your attention

Malaria Prophylaxis: PICO questions

What are the harms related to malaria prophylaxis with Mefloquine or Malarone or Doxycycline in travellers?

Population: Travellers to malaria areas

Intervention: Mefloquine or Malarone or Doxycycline

Comparison: Mefloquine or Malarone or Doxycycline or Placebo

Harms:

Serious adverse events:

- Cardiac
- Neuropsychiatric
- Benign intracranial hypertension with visual changes
- Serious skin reactions
- Discontinuation of drug

Minor:

- Dermatologic
- Gastrointestinal

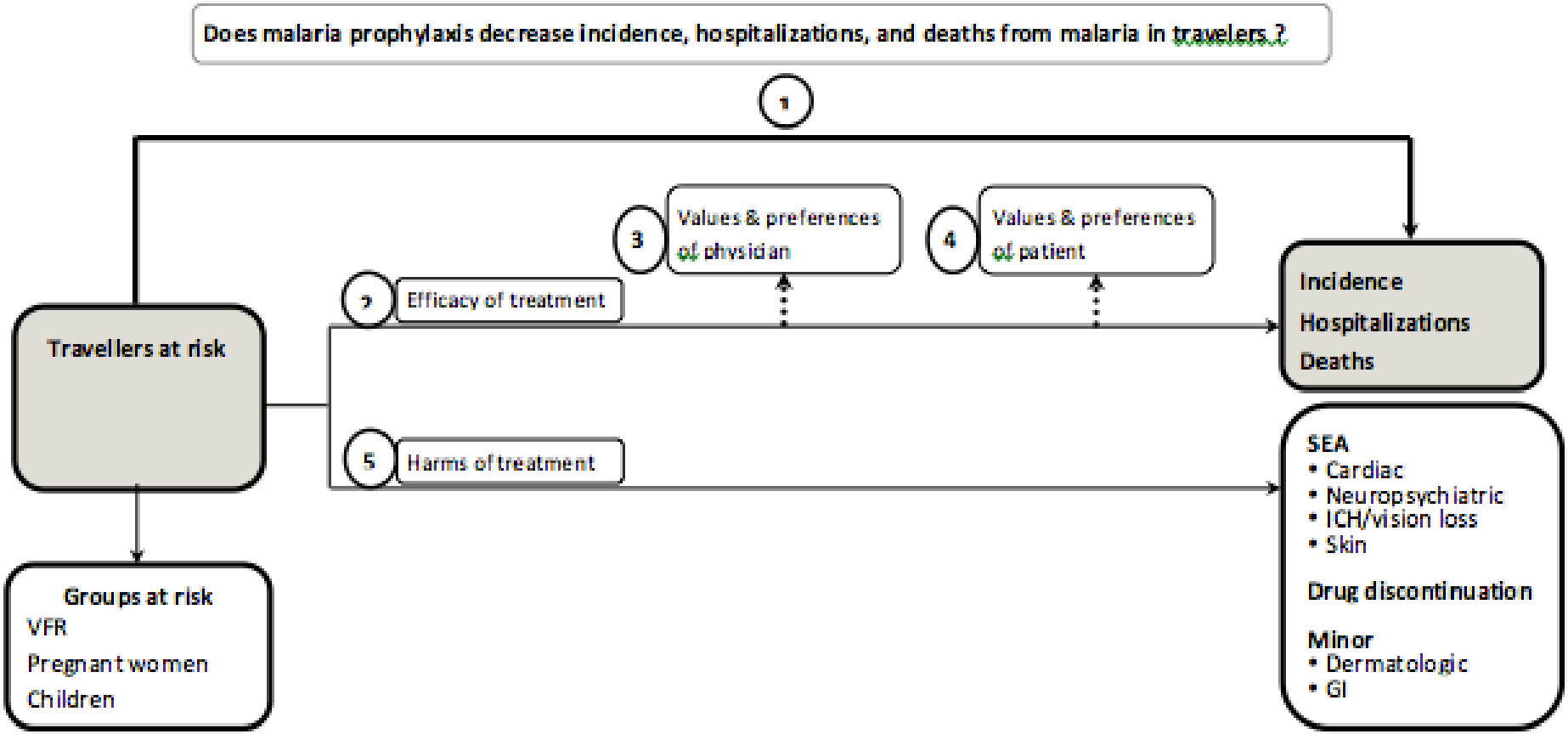

Does malaria prophylaxis decrease incidence, hospitalizations, and deaths from malaria in travelers ?
1
Travellers at risk
2
Efficacy of treatment
3
Values & preferences of physician
4
Values & preferences of patient
Incidence
Hospitalizations
Deaths
5
Harms of treatment
SEA
• Cardiac
• Neuropsychiatric
• ICH/vision loss
• Skin
Drug discontinuation
Minor
• Dermatologic
• GI
Groups at risk
VFR
Pregnant women
Children

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Table. Estimates (by study) of malaria rates for travelers to various destinations. Estimates are of number of trips x 1,000 per reported malaria case. For example, 157.4 represents an estimate of 1 malaria case/157,400 trips.

Study	All Asia	SE Asia	South Asia	SS Africa	East Africa	West Africa	C. Africa	PNG	Carib.	Central Amer.	Middle East	Mex.	South Amer.
Tada et al 2008 (Japan)	157.4	204.1	24.9	2.5	4.6	1.3	4.7	0.7	/	/	/	/	/
Romi et al 2010 (Italy)	12.5	/	/	0.8	1.7	0.7	/	/	/	/	/	/	/
Spencer et al 2009 (USA)	12.6	/	/	0.7	/	/	/	0.3	28	17.2	149.6	813	44.3
Askling et al. 2005 (Sweden)	/	18.5	1.6	0.4	0.4	0.3	0.3	/	/	78.6	55	/	/
Massad et al 2011	/	/	9.0	/	/	0.5	/	/	/	/	/	/	/
Broderick et al 2015 (UK)	/	/	8.3	/	/	/	/	/	/	/	/	/	/
Berhens et al 2010	/	111		/	/	/	/	/	/	/	/	/	/
Crude estimate	60.8 ± 48.3	111.2 ± 53.6	11.0 ± 4.9	1.1 ± 0.5	2.2 ± 1.2	0.7 ± 0.2	2.5 ± 2.2	0.5 ± 0.2	28	47.9 ± 30.7	102.3 ± 47.3	813	44.3