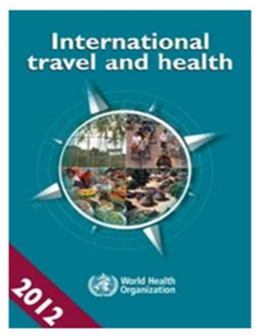
Malaria: when the need for chemoprophylaxis is not clear-cut

Dr Ula Maniewski

11th National Seminar on Travel Medicine

Thursday 19th November 2015



ABCDE of malariaprevention for travellers

- **A**: Awareness
- **B**: Bite prevention
- **C:** Chemoprophylaxis, if indicated.
- **D**: Diagnosis
- **E**: Environment: Avoid outdoor activities in environments that are mosquito breeding places, especially in late evenings and at night.

Malaria prevention

- Chemoprophylaxis
  - Atovaquone/proguanil (-1d;+7d)
  - Mefloquine 1/w (-2w;+4w)
  - Doxycycline 100 mg 1/d (-1d;+28d)
  - Chloroquine 300 mg 1x/w (-1w;+4w)

REVIEW ARTICLE

Who Needs Drug Prophylaxis against Malaria? My Personal View

Lars Rombo

A long tradition of successful malaria prophylaxis with chloroquine led to a dogma that drug prophylaxis should be given regardless of risk as soon as a traveler entered endemic areas. This prevailed also when resistance to chloroquine and adverse effects of alternatives became a problem. A cost/benefit analysis of the risk for malaria versus risk for adverse effects and cost of the recommended drug is not uniformly applied and drug prophylaxis is still advocated even when the risk for severe adverse effects greatly exceeds the risk for malaria, which is unethical.

J Travel med, 2005

In low malaria risk areas, whether or not prescribing chemoprophylaxis is not always a clear-cut decision

The choice of prevention depends on:

1) Risk to get malaria

- Depends on the region, but can vary locally
- Depends on activities (how to spend evenings/ nights)
- Can vary in different seasons
- Can vary between locals-travellers-expats

2) Which type of malaria one expects (P falciparum, P non falciparum, resistance)

In low malaria risk areas, the advice is nuanced, taking into account the preferences of the traveller

Voumard et al. Malaria Journal (2015) 14:139
DOI 10.1186/s12936-015-0654-y

RESEARCH **Open Access**

Switzerland

Recommendations for malaria prevention in moderate to low risk areas: travellers' choice and risk perception

Rachel Voumard[1], Delphine Berthod[2], Clotilde Rambaud-Althaus[3], Valérie D'Acremont[1,3] and Blaise Genton[1,2,3*]

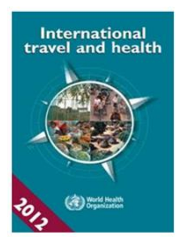
Abstract

When travelling to moderate- to low-risk malaria areas, **85%** of interviewees **chose not to take** chemoprophylaxis as malaria prevention, although most (*non-Swiss*) guidelines recommend it.

*… hence **15 %** of interviewees **chose to take** chemoprophylaxis as malaria prevention, although Swiss guidelines **do not** recommend it…*

They had coherent reasons for their choice.

New recommendations should include **shared decision-making** to take into account **travellers' preferences**.



Malaria risk and type of prevention

Belgian Consensus

	Malaria risk	Type of prevention
Type A	Very limited risk of malaria	Mosquito bite prevention only transmission
Type B A/B	Risk of *P. vivax* malaria ~~only~~ or (very) low risk of P falciparum	Mosquito bite prevention plus chloroquine or d… ch… se… contraindications) Mosquito bite prevention + think of malaria when T° + /- chemoprophylaxis intermittent or SBET
Type C	Risk of *P. falciparum* with reported chloroquine and sulfadoxine–pyrimethamine resistance	Mosquito bite prevention plus malaria, atovaquone–proguanil or doxycycline or mefloquine chemoprophylaxis (select according to reported side-effects and contraindications)[a]
Type D	~~Risk of *P. falciparum* malaria in combination with reported multidrug resistance~~	Mosquito bite prevention plus atovaquone–proguanil or doxycycline or mefloquine chemoprophylaxis (select according to reported drug resistance pattern, side-effects and contraindications)[a,b]

[a]Alternatively, for travel to rural areas with low risk of malaria infection, mosquito bite prevention can be combined with stand-by emergency treatment (SBET).

Belgian Consensus 2015

"In most regions in Asia & Latin America (see map of the German-speaking countries: http://www.dtg.org/21.0.html), one can decide not to take continuously malaria tablets (chemoprophylaxis) after a thorough evaluation of the risk. The malaria risk is mostly low to negligible, even for adventurous travellers and/or long term travelers, and depends on the specific region, the season, rural vs urban stay, but foremost on the quality of accommodation for the night, and on the availability of a good quality local health care providing reliable malaria diagnosis and appropriate treatment. It is imperative to avoid always mosquito bites between sunset and sunrise, by means of repellents and mosquito nets. A fever that appears during or after travel to a region with a low malaria risk may still be due to malaria. This diagnosis has to be ruled out, even if the absolute risk is very low.
In case different regions are visited (with a generally low regional malaria-risk, but probably locally more elevated malaria risk) there are some more options besides continuous malaria chemoprophylaxis.
A "standby emergency treatment (SBET)" (e.g. atovaquone/proguanil) can be carried in the travel kit with complete instructions how and when to use.
and/or a planning for the temporarily malaria chemoprophylaxis (atovaquone/proguanil) based on the regional malaria risk , when the malaria risk in the region visited is sufficiently high (information on www.itg.be)."

Which strategies exist in low malaria risk areas?

GERMAN SPEAKING EUROPE

- Bite prevention always
- AND think of malaria when sick

- Standby emergency treatment

BELGIUM

- Bite prevention always
- AND think of malaria when sick

- Chemoprophylaxis when risk is locally/ circumstances higher
- SBET in some cases

Countries with ongoing transmission of malaria, 2013

International travel and health

2012

World Health Organization

Confirmed malaria cases per 1000 population

- >100
- 50-100
- 10-50
- 1-10
- 0.1-1
- 0-0.1
- Non-endemic or no ongoing malaria transmission
- Not applicable

0 875 1'750 3'500 Kilometers

Malariaprophylaxe 2015

Einteilung in Zonen mit unterschiedlicher medikamentöser Chemoprophylaxe gemäß den Empfehlungen der DTG - Deutschen Gesellschaft für Tropenmedizin und Internationale Gesundheit

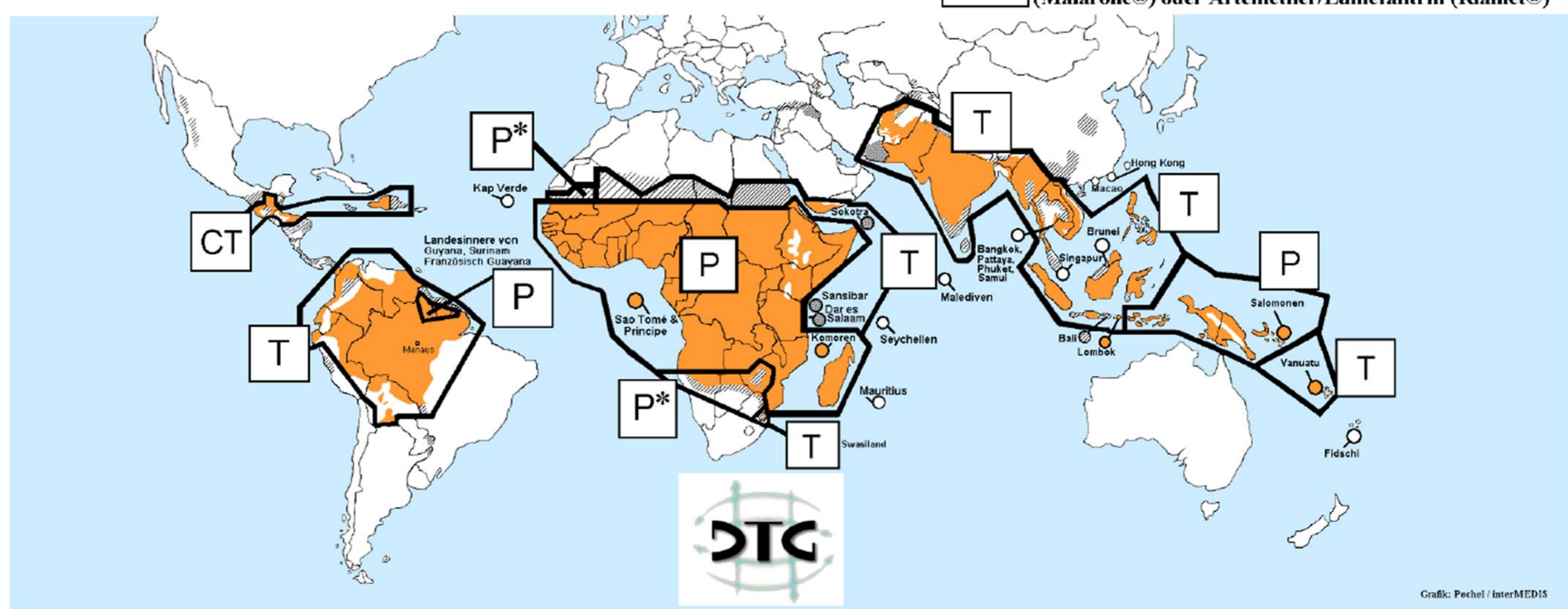
Stand: April 2015

Für alle Malariagebiete gilt:

Mückenschutz empfohlen (minimales Risiko siehe Länderliste)

- **Gebiete, wo die Malaria nicht oder nicht mehr vorkommt**
- **Gebiete mit sehr beschränktem Malariarisiko: Malariaübertragung selten**
- **Gebiete mit Malariaübertragung**

P	**Zur Chemoprophylaxe Atovaquon/Proguanil (Malarone®) oder Doxycyclin* oder Mefloquin (Lariam ®)** * Für diese Indikation in Deutschland nicht zugelassen ** Besondere Warnhinweise beachten
T	**Zur Notfalltherapie Atovaquon/Proguanil (Malarone®) oder Artemether/Lumefantrin (Riamet ®) Keine Chemoprophylaxe empfohlen**
CT	**Chloroquin zur Notfalltherapie Keine Chemoprophylaxe empfohlen**
P*	**Chemoprophylaxe saisonal empfohlen mit Atovaquon/Proguanil (Malarone®) oder Doxycyclin* oder Mefloquin (Lariam®)** * Für diese Indikation in Deutschland nicht zugelassen ** Besondere Warnhinweise beachten **Ansonsten Notfalltherapie Atovaquon/Proguanil (Malarone®) oder Artemether/Lumefantrin (Riamet®)**



Angepasst an WHO, World Malaria Report 2014, WHO International Travel And Health 2014, Swiss TPH, Basel/ B.R. Beck; Universität Zürich/ISPMZ; M. Funk

Malaria 2015 *(source WHO 2010, World Malaria Report 2014)*

A/B A/C A/B A A C A A/C A

- no risk
- limited risk
- elevated risk

A Mosquito bite prevention only / **B** Nivaquine® weekly

C Malarone® or doxycycline daily; Lariam® weekly

for details : see www.itg.be

RESEARCH Open Access

Declining incidence of imported malaria in the Netherlands, 2000-2007

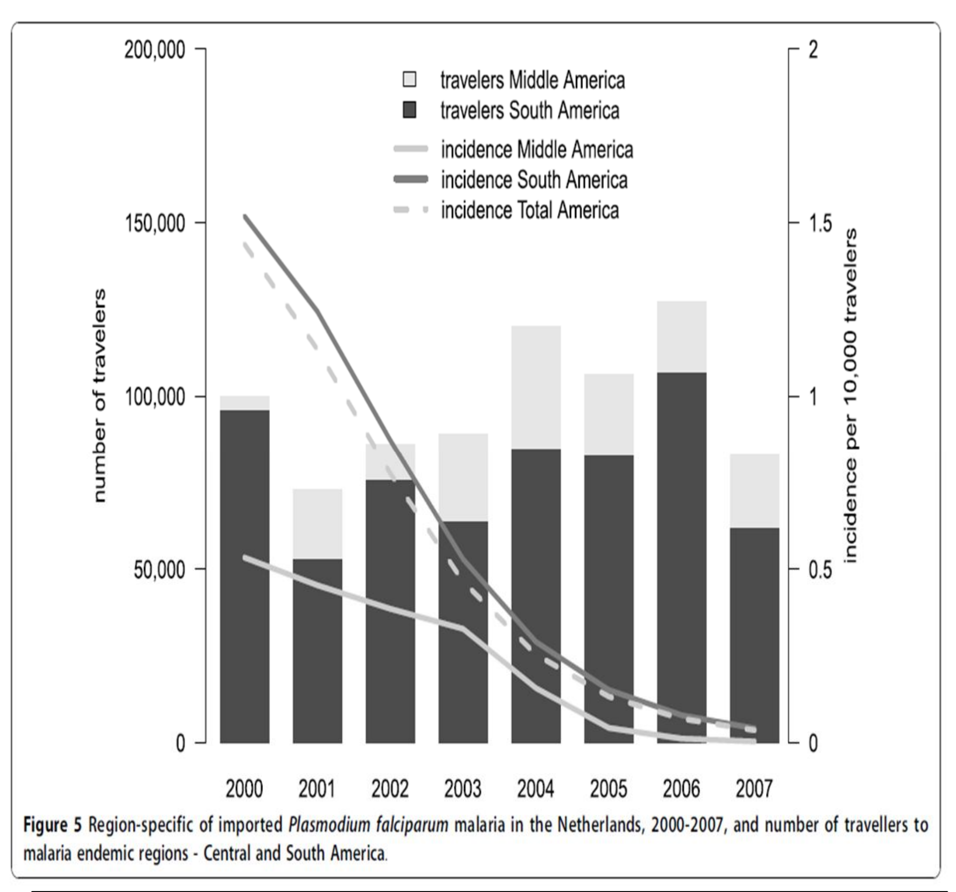


Figure 5 Region-specific of imported *Plasmodium falciparum* malaria in the Netherlands, 2000-2007, and number of travellers to malaria endemic regions - Central and South America.

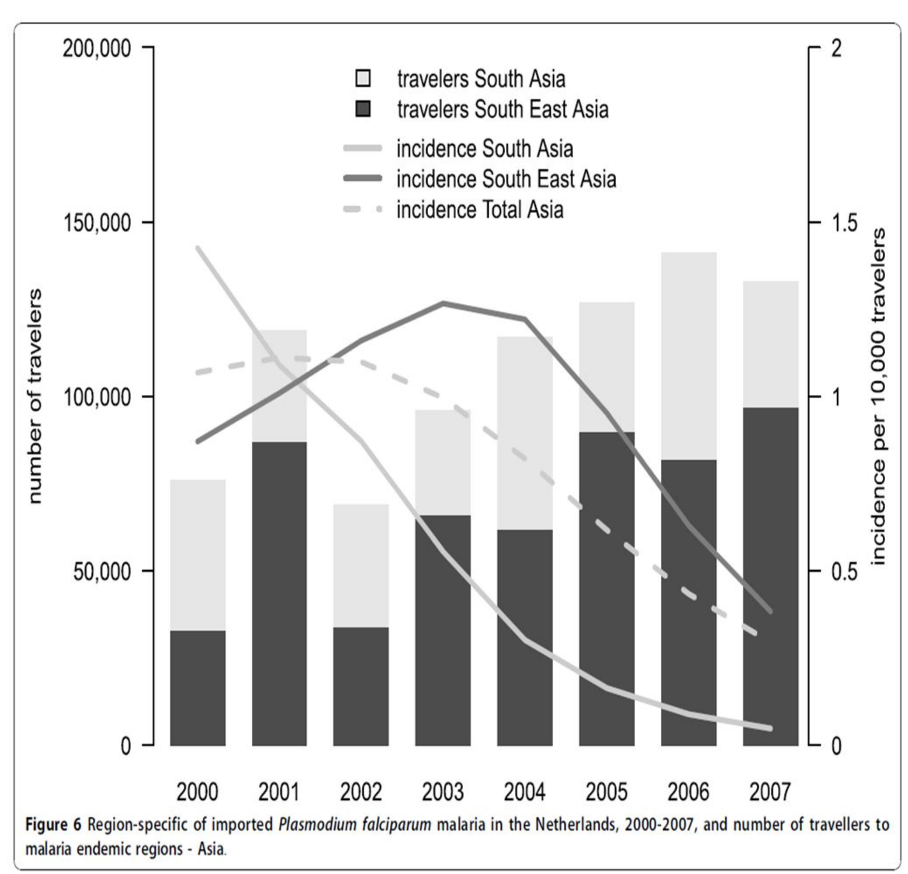


Figure 6 Region-specific of imported *Plasmodium falciparum* malaria in the Netherlands, 2000-2007, and number of travellers to malaria endemic regions - Asia.

Americas: risk 1/100,000

Asia: risk 1-4/100,000

Van Rijckevorsel et al. *Malar J* 2010

RESEARCH Open Access

Declining incidence of imported malaria in the Netherlands, 2000-2007

travelers Middle and West Africa
travelers East and Southern Africa
incidence Middle and West Africa
incidence East and Southern Africa
incidence Total Africa

number of travelers: 0, 50,000, 100,000, 150,000, 200,000

incidence per 10,000 travelers: 0, 50, 100, 150, 200

2000 2001 2002 2003 2004 2005 2006 2007

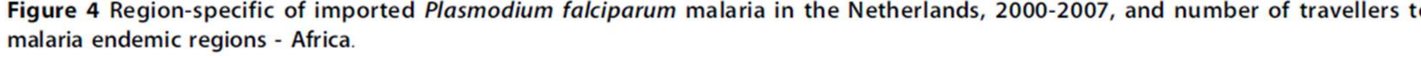
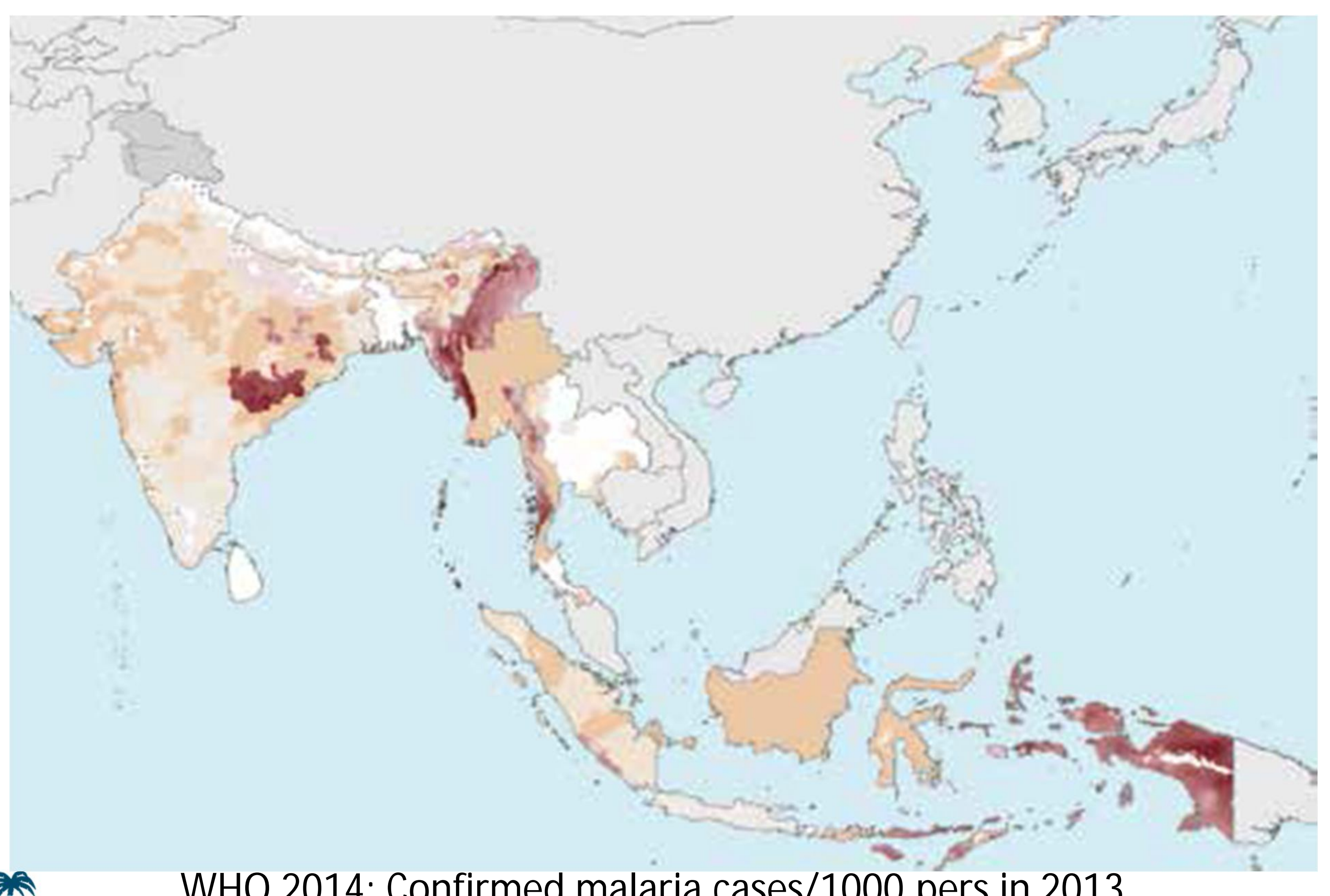


Figure 4 Region-specific of imported *Plasmodium falciparum* malaria in the Netherlands, 2000-2007, and number of travellers to malaria endemic regions - Africa.

Africa: risk 10-400/100,000

Van Rijckevorsel et al. *Malar J* 2010

Some examples in Asia



WHO 2014: Confirmed malaria cases/1000 pers in 2013

India

Tropimed US: risk in all areas < 2000m

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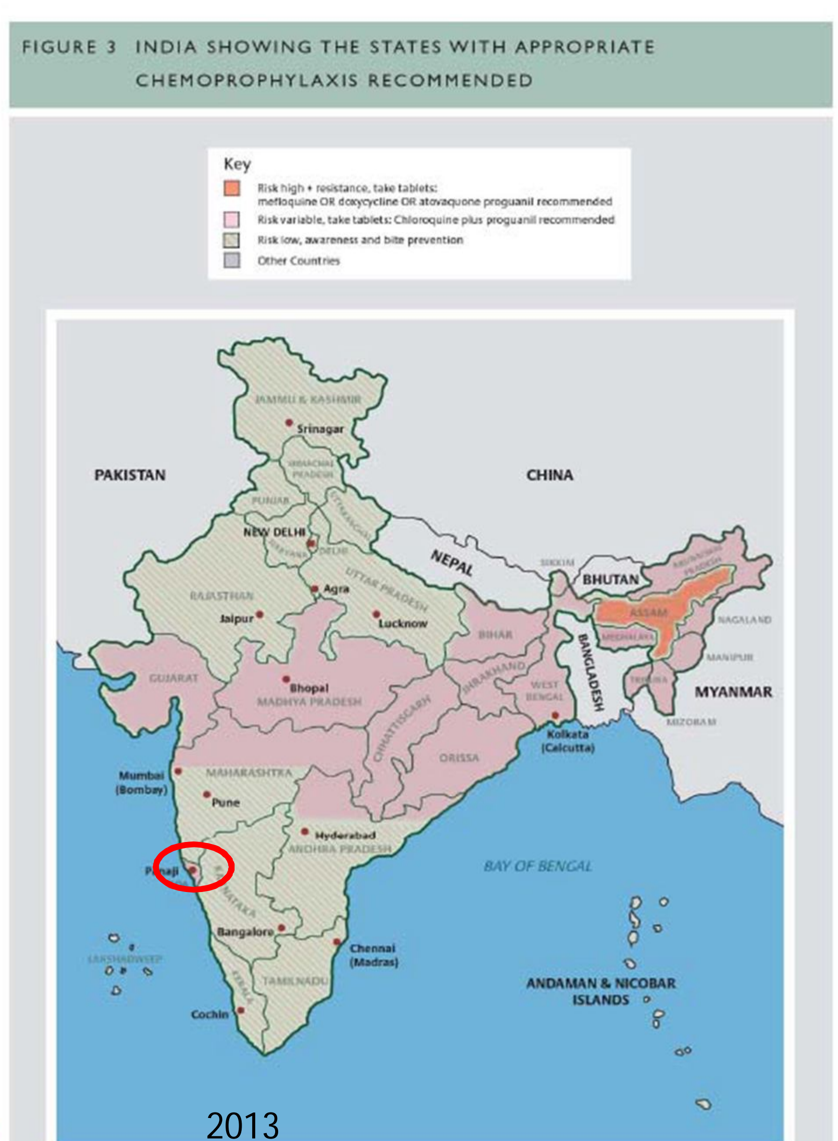
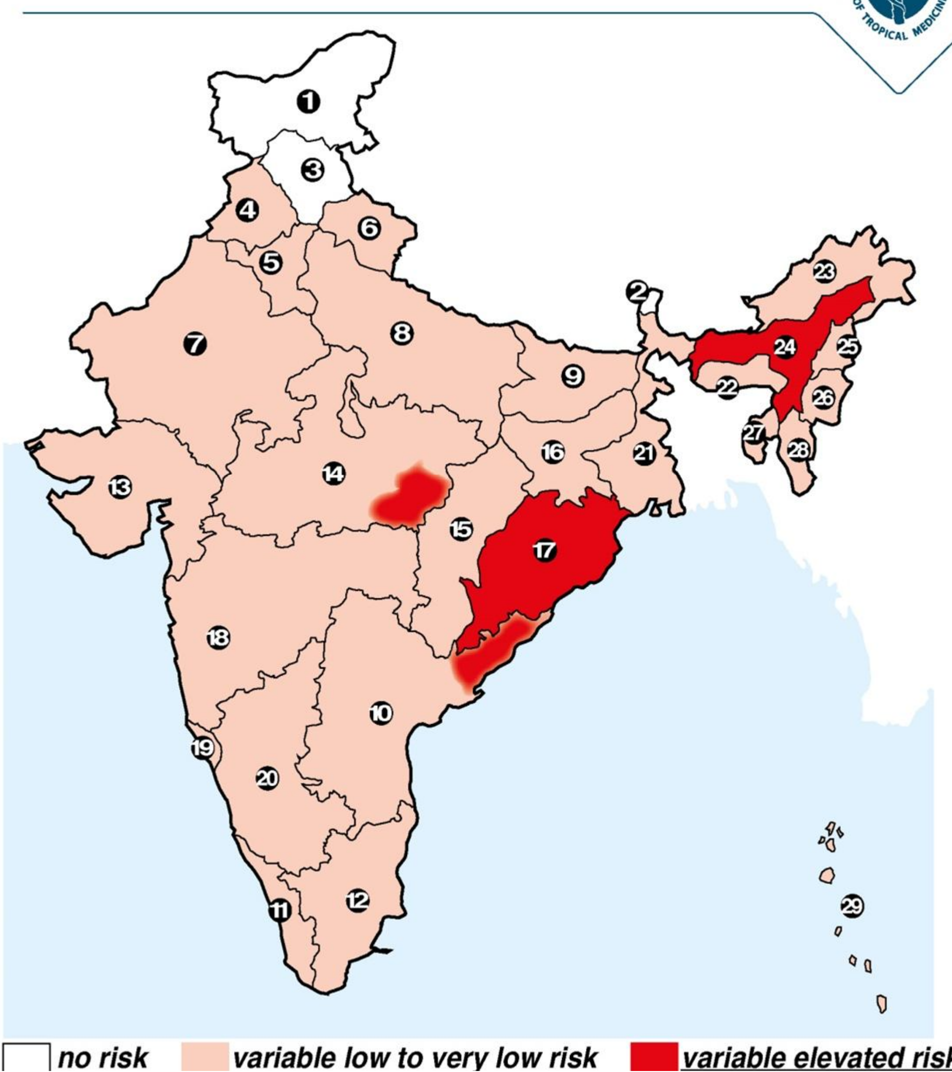
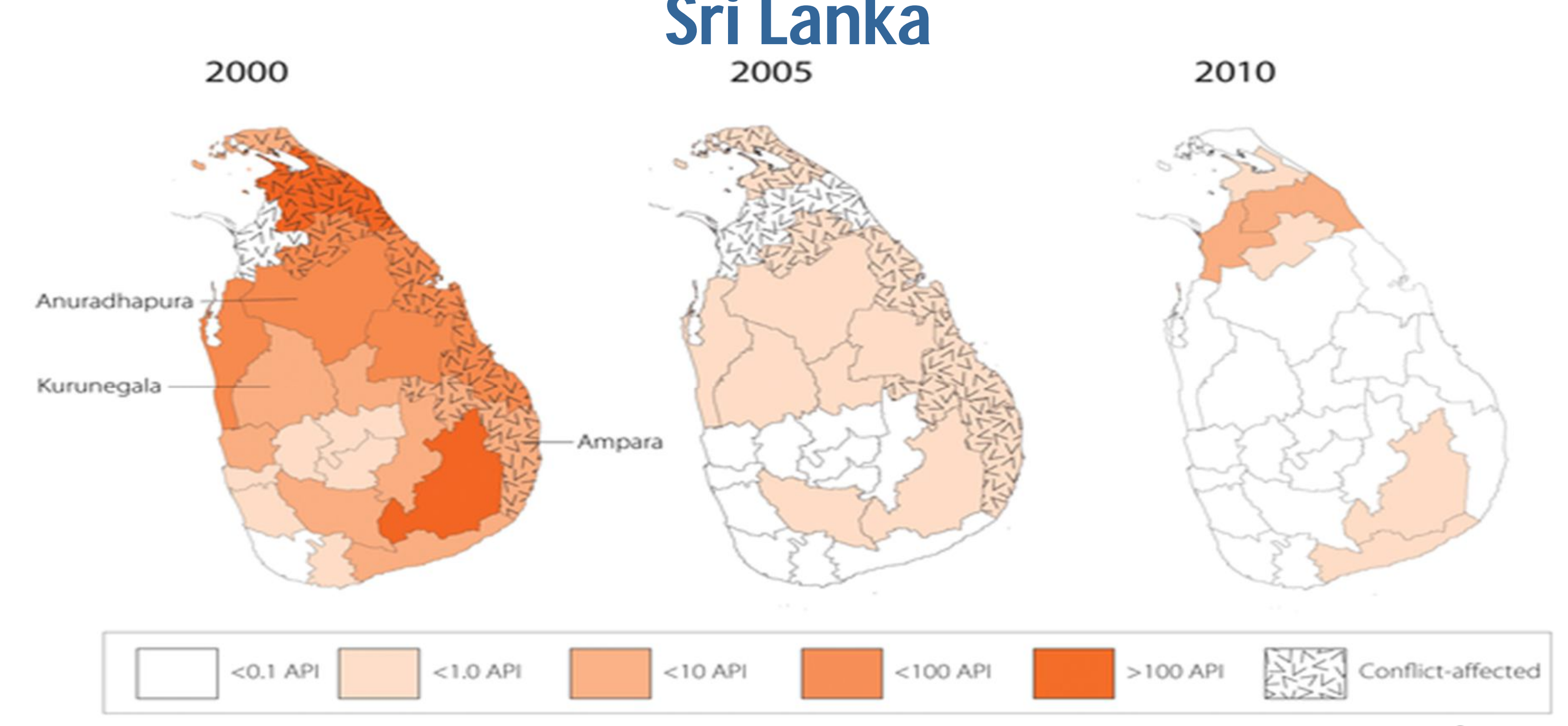
UK guidelines





“ Het risico voor **resistente falciparum malaria** kan hoog zijn in
de staat *Assam*, *Orissa*
een klein gedeelte van de staat *Andhra Pradesh*, een klein gedeelte van de staat *Madhya*
Hier is de inname van malariatabletten aangewezen zoals in zone C.”

Sri Lanka



http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0043162

PLOS | ONE

WHO 2015: no malaria cases locally acquired since oct 2012. Before 88% P vivax

Viet Nam

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ITG, 2015

Indonesia

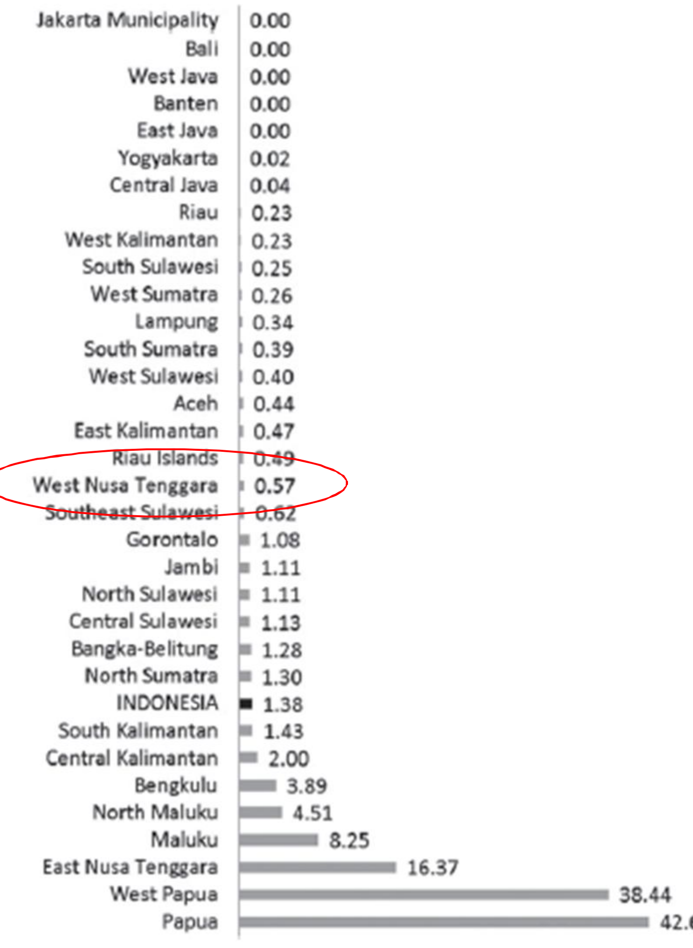
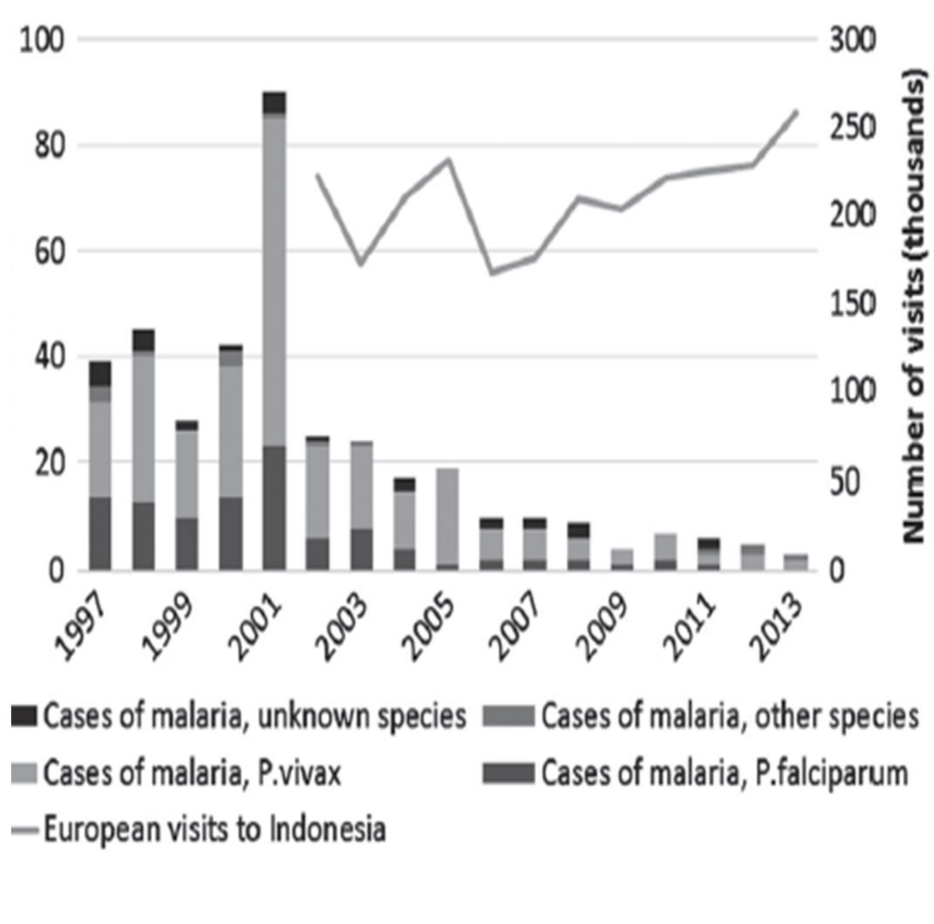


Figure 2 Annual Parasite Index (API) per province and compared with country total API, 2013 (data from Indonesian MoH).



J Travel Med 2015; 22: 389–395

Indonesia WHO report 2010

Malaysia

Indian Ocean

Australia

Insufficient data | 0 | 0–0.1 | 0.1–1.0 | 1.0–10 | 10–50 | 50–100 | ≥100

Distribution of confirmed malaria cases (per 1 000 population)

Thailand
Malaysia
South China Sea
Brunei
Pacific Ocean
Medan
Malaysia
Celebes Sea
Singapour
Manadao
Padang
Borneo isl.
Kalimantan
Sorong
Biak
Jayapura
Papua Barat
Papua
Sumatra
Sulawesi
Palopo
Banjarmasin
Ambon
Jakarta
Java Sea
Ujung Pandang
Banda Sea
Bandung
Java
Bali
Yogyakarta
Arafura Sea
Indian Ocean
Flores Sea
660 km
0
2cm

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Nusa Tenggara Barat
Bali
Lombok
Sumbawa
Flores
Lomblen
Alor
Wetar
Denpasar
Mataram
Raba
Ruteng
Pantar
East Timor
Sumba
Waingapu
Sawu Sea
Timor
Kupang
Sawu

Indonesia

Malaria Endemic Areas

- **Risk areas**
  all areas of eastern Indonesia (prov. of Maluku, Maluku Utara, Nusa Tenggara Timur, Papua, and Papua Barat) incl. town of Labuan Bajo and Komodo Islands in the Nusa Tengarra region; rural areas of Kalimantan (Borneo), Nusa Tenggara Barat (incl. the island of Lombok), Sulawesi, and Sumatra
- **Low transmission** in rural areas of Java incl. Pangandaran, Sukalumi, and Ujung Kulong
- **Malaria-free**
  Jakarta, Ubud, resort areas of Bali and Java, and Gili Islands, and the Thousand Islands (Pulau Seribu)

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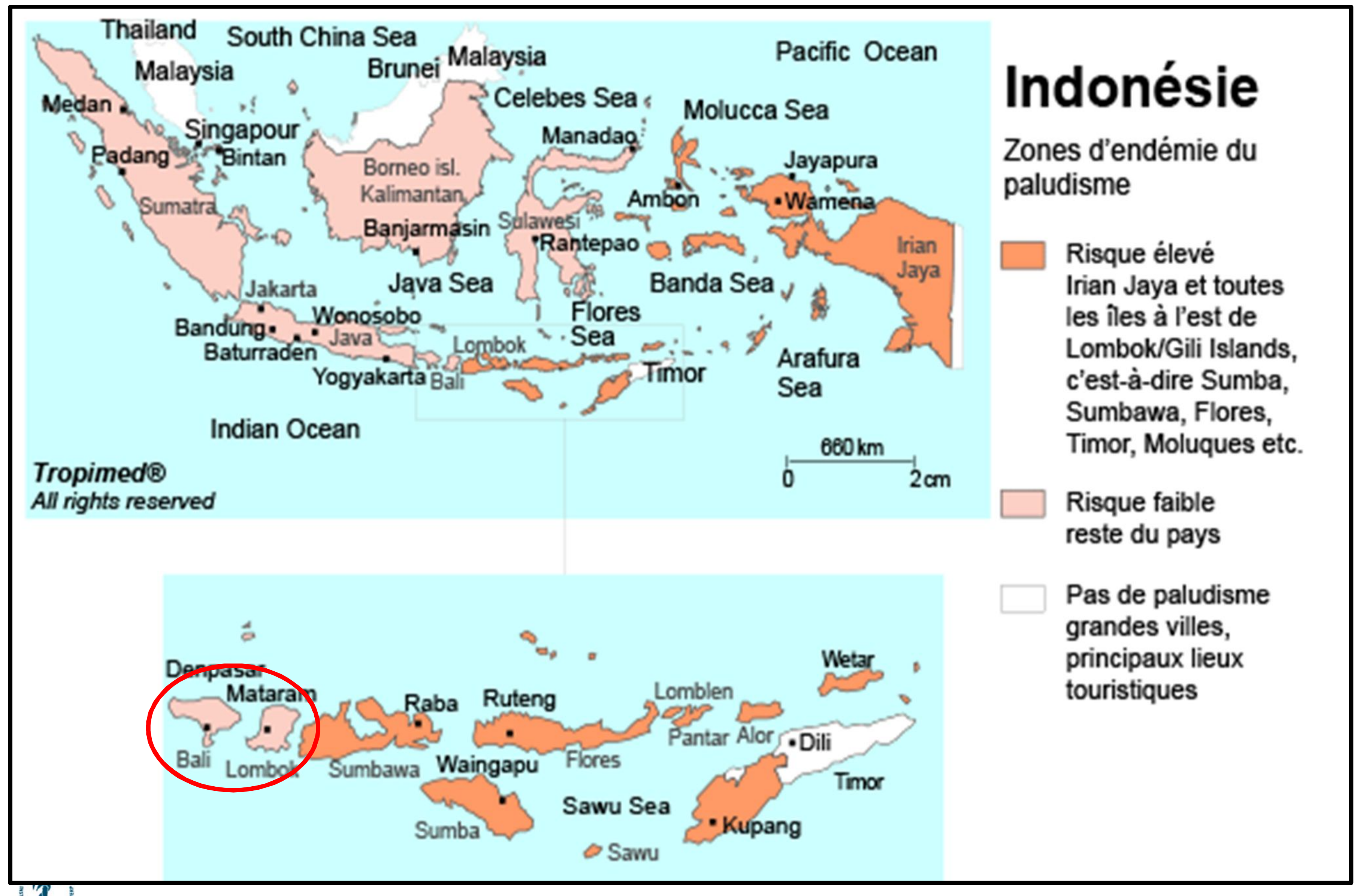
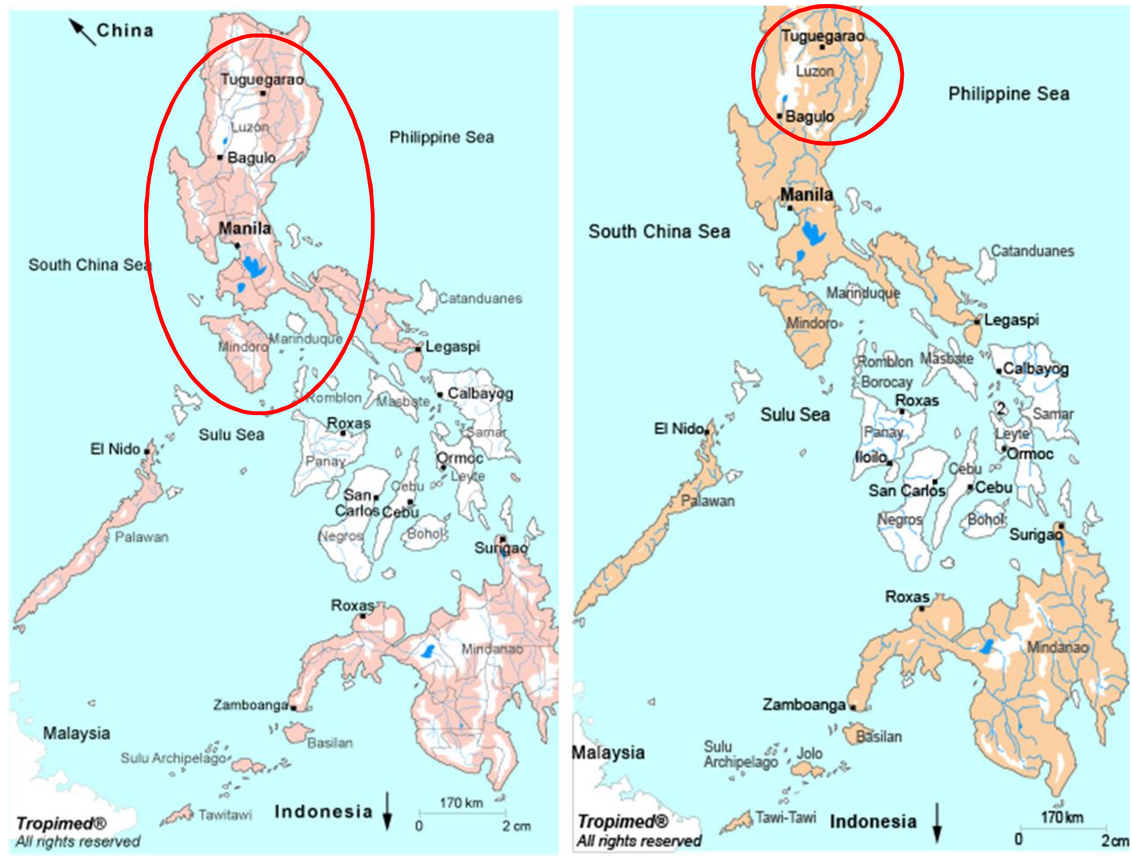


Philippines



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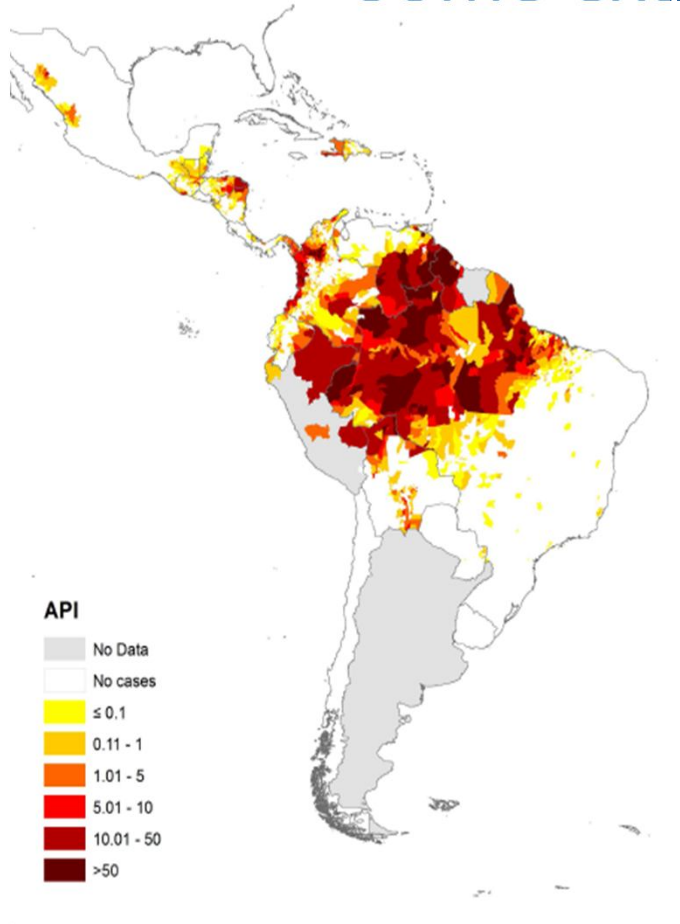
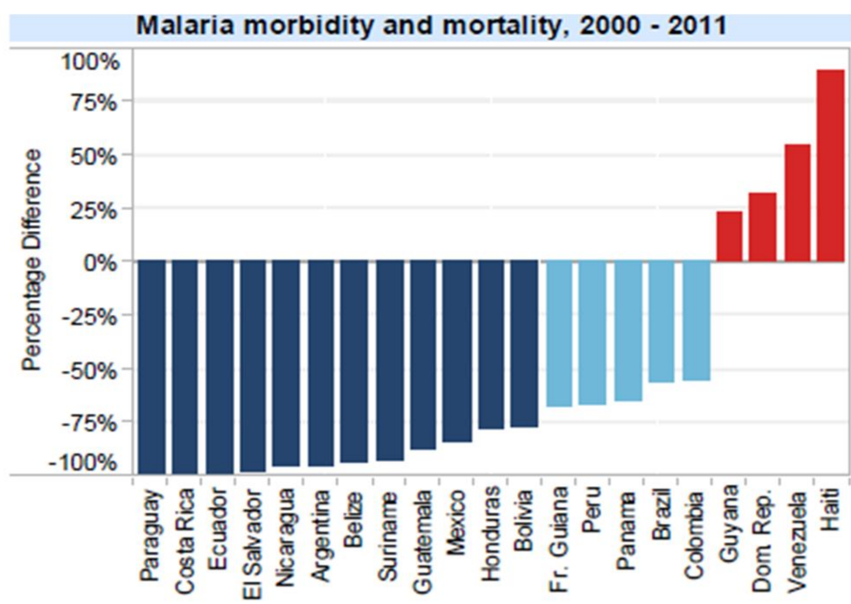
WHO 2014

Travax 2015

Some examples in South America





Malaria Journal

Opinion

Open Access

The low and declining risk of malaria in travellers to Latin America: is there still an indication for chemoprophylaxis?

Ron H Behrens*[1,2], Bernadette Carroll[1], Jiri Beran[3], Olivier Bouchaud[4], Urban Hellgren[5], Christoph Hatz[6], Tomas Jelinek[7], Fabrice Legros[8], Nikolai Mühlberger[9], Bjørn Myrvang[10], Heli Siikamäki[11], Leo Visser[12] for TropNetEurop

Bolivia

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Bolivia

Malaria Endemic Areas

- Risk in all areas <2,500 m (<8,202 ft)
- Malaria-free including city of La Paz

National Park NP
Integrated Management Natural Area IMNA
Wildlife National Reserve WNR

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Bolivie

Zones d'endémie du paludisme

- Risque faible < 2500 m
  Paludisme dû aux *P. falciparum* à Santa Cruz et dans les départements du nord Beni et Pando, surtout dans les villes de Guayaramerin, Itinez et Riberalta
- Pas de paludisme
  villes, provinces Oruro et Potosi

Parc National PN
Aire Naturelle de Gestion Intégrée ANGI
Réserve Nationale de la Vie Sauvage RNVS

Aires protégés

1	Sajama PN/ANGI	13	Pilón Lajas ANGI
2	Tunari PN	14	El Palmar ANGI
3	Isiboro Sécure PN	15	San Matías ANGI
4	Noel Kempff PN	16a	Amboró PN
5	Torotoro PN/ANGI	16b	Amboró ANGI
6	Carrasco PN	17	Cotapata PN/ANGI
7	Eduardo Avaroa RNVS	18	Madidi PN
8	Manuripi RNVS	19a	Kaa Iya PN
9	Tariquía RNVS	19b	Kaa Iya ANGI
10	Sama RNVS	20a	Otuquis PN
11	Apolobamba ANGI	20b	Otuquis ANGI
12	EBB ANGI	21	Aguaragüe PN/ANGI

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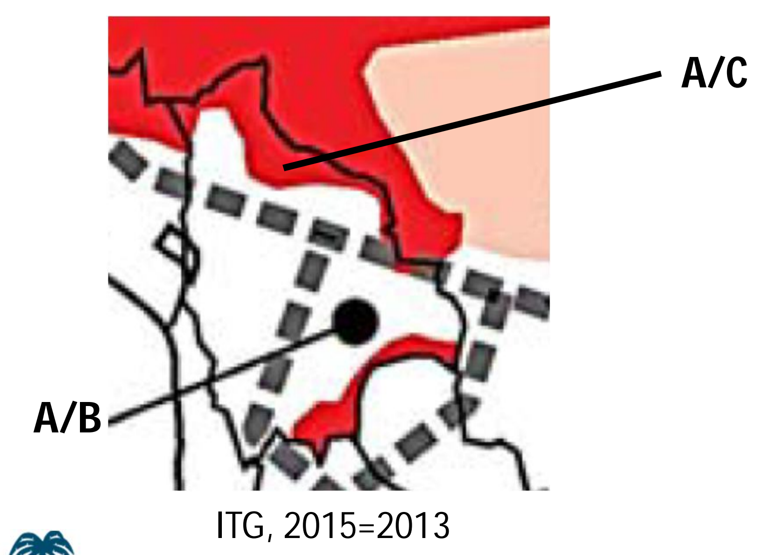
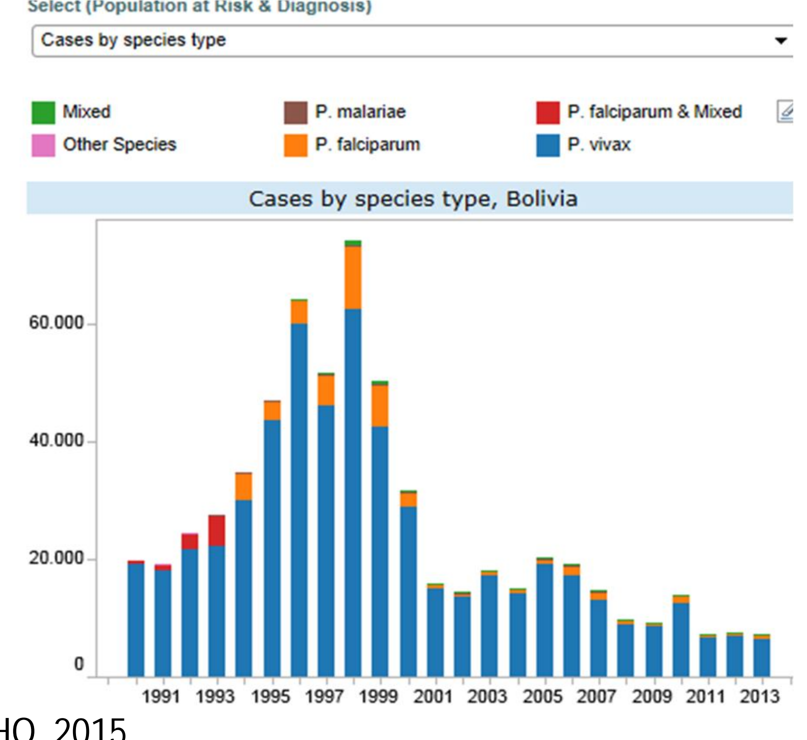
Bolivia

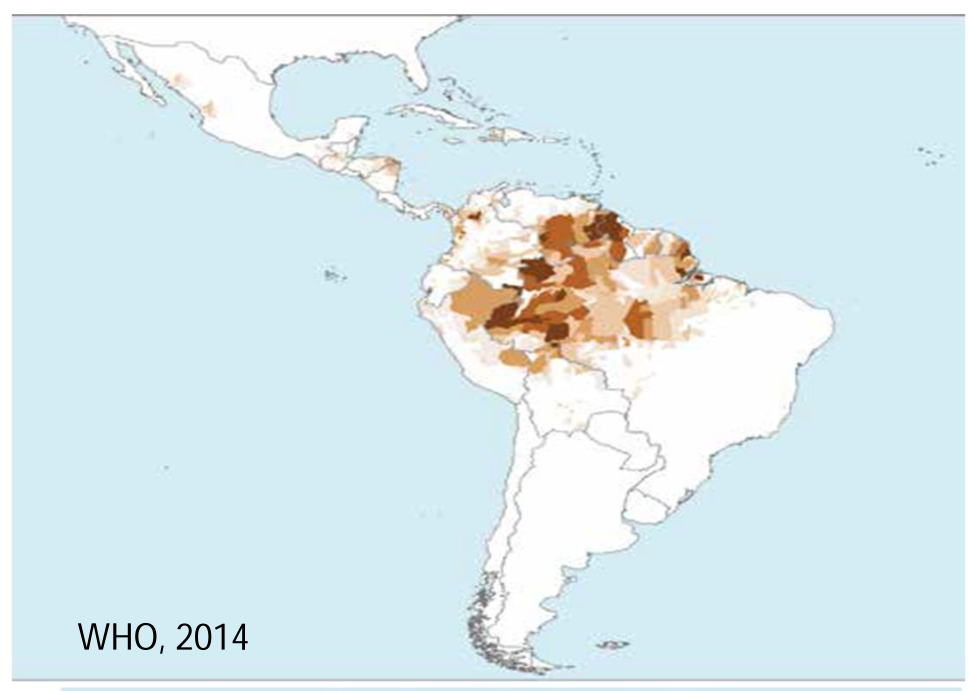


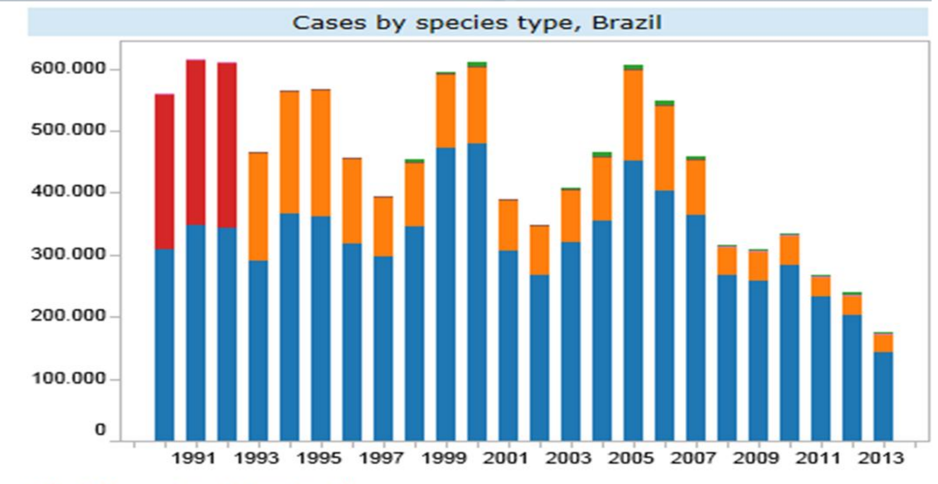
ITG, 2015=2013



PAHO, 2015

Brazil

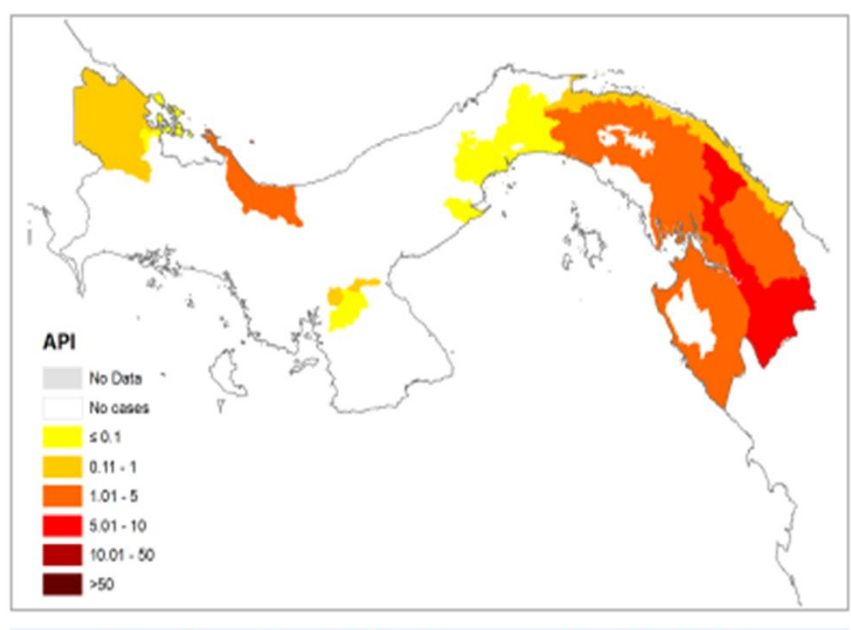

WHO, 2014

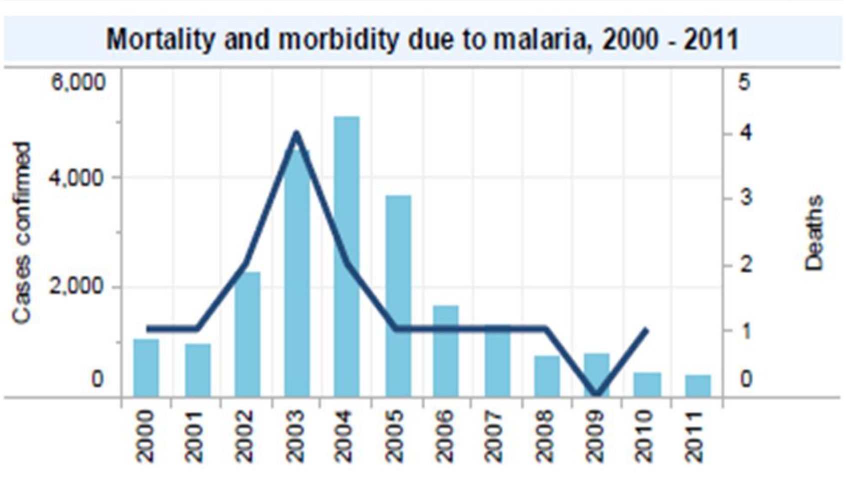


PAHO, 2015

UK, 2013

Panama





PAHO, 2015

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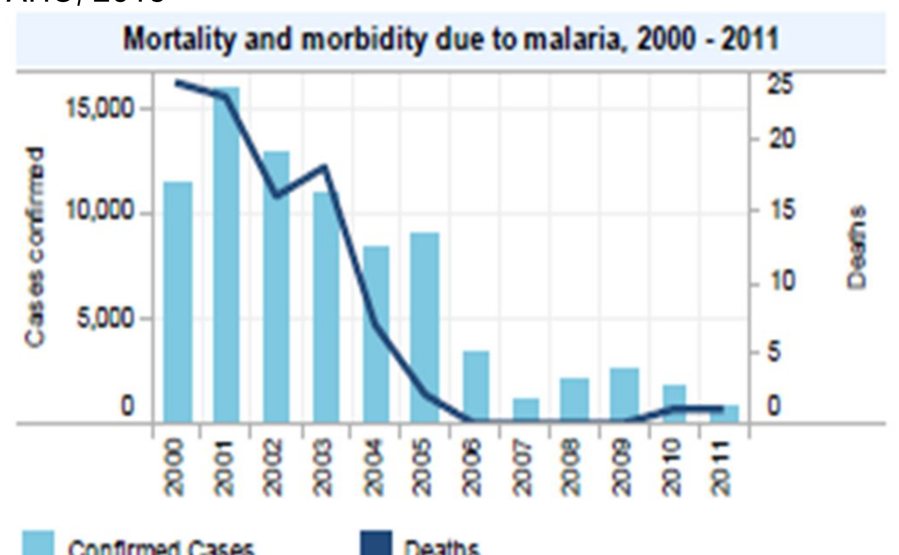
Low to no risk antimalarials not usually advised

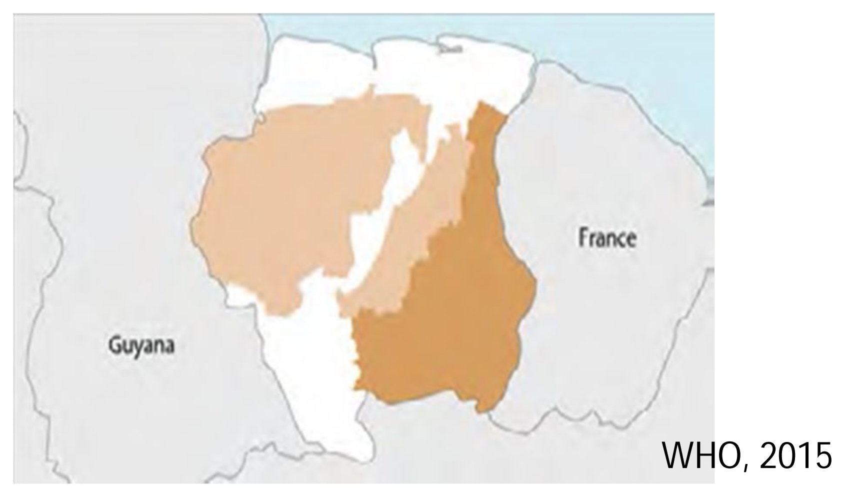
Surrounding countries with malaria risk

Fitfortravel, 2015

Suriname

PAHO, 2015





WHO, 2015

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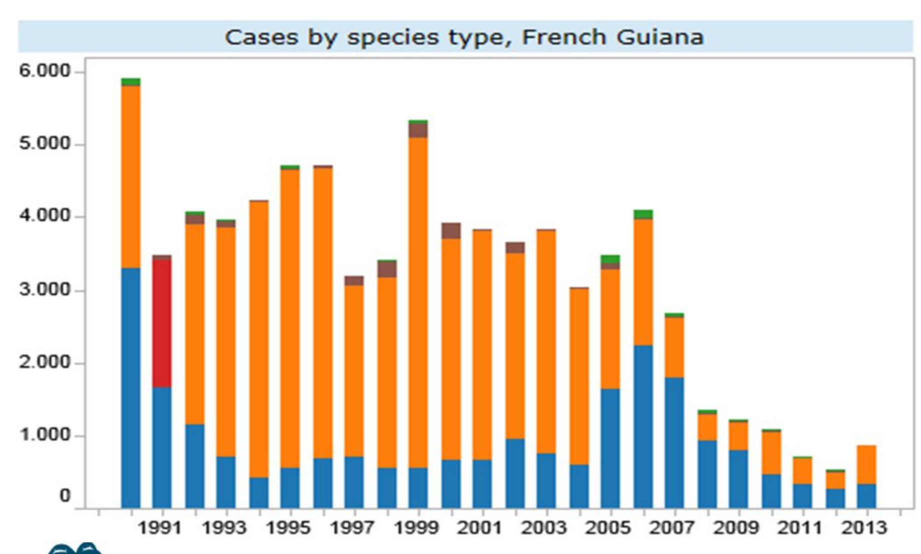
LCI, Van Ginderen, CISTM 14

French Guyane

WHO, 2014



PAHO, 2015

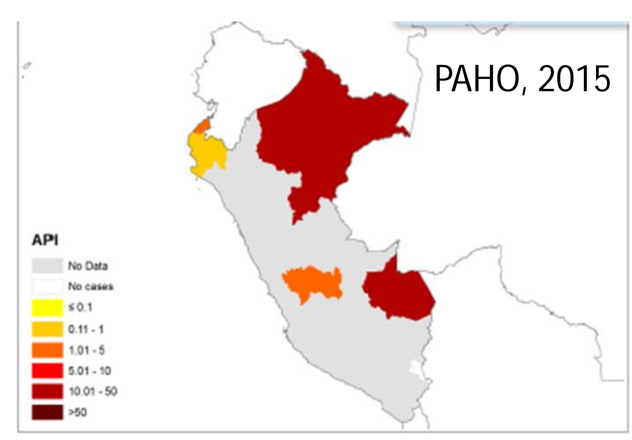
LE RISQUE PALUDISME EN GUYANE
septembre à mars

OCEAN ATLANTIQUE
SURINAME
BRESIL

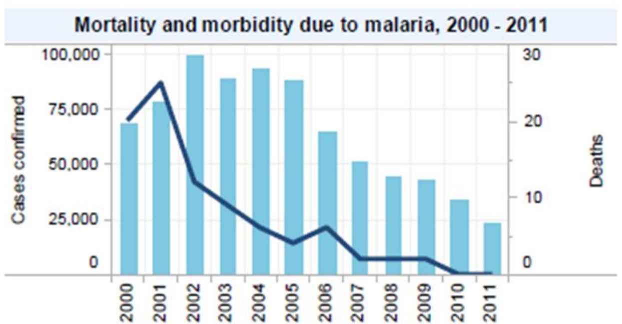
ARS, Guyane, 2015

Peru

WHO, 2014



PAHO, 2015



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Bedankt voor uw aandacht