
LE VACCINAZIONI PEDIATRIC
E DEGLI ADULTI:
I PIÙ RECENTI AGGIORNAME
CAGLIARI TH
14 APRILE 2018

Conflicts of interest

2017

Advisory Board Meeting Sanofi

Advisory Board Meeting PaxVax

2018

None to declare

La profilassi del viaggiatore internazionale

Andrea Rossanese

entro Malattie Tropicali, Negrar (VR)

President-Elect, SIMVIM

AGENDA

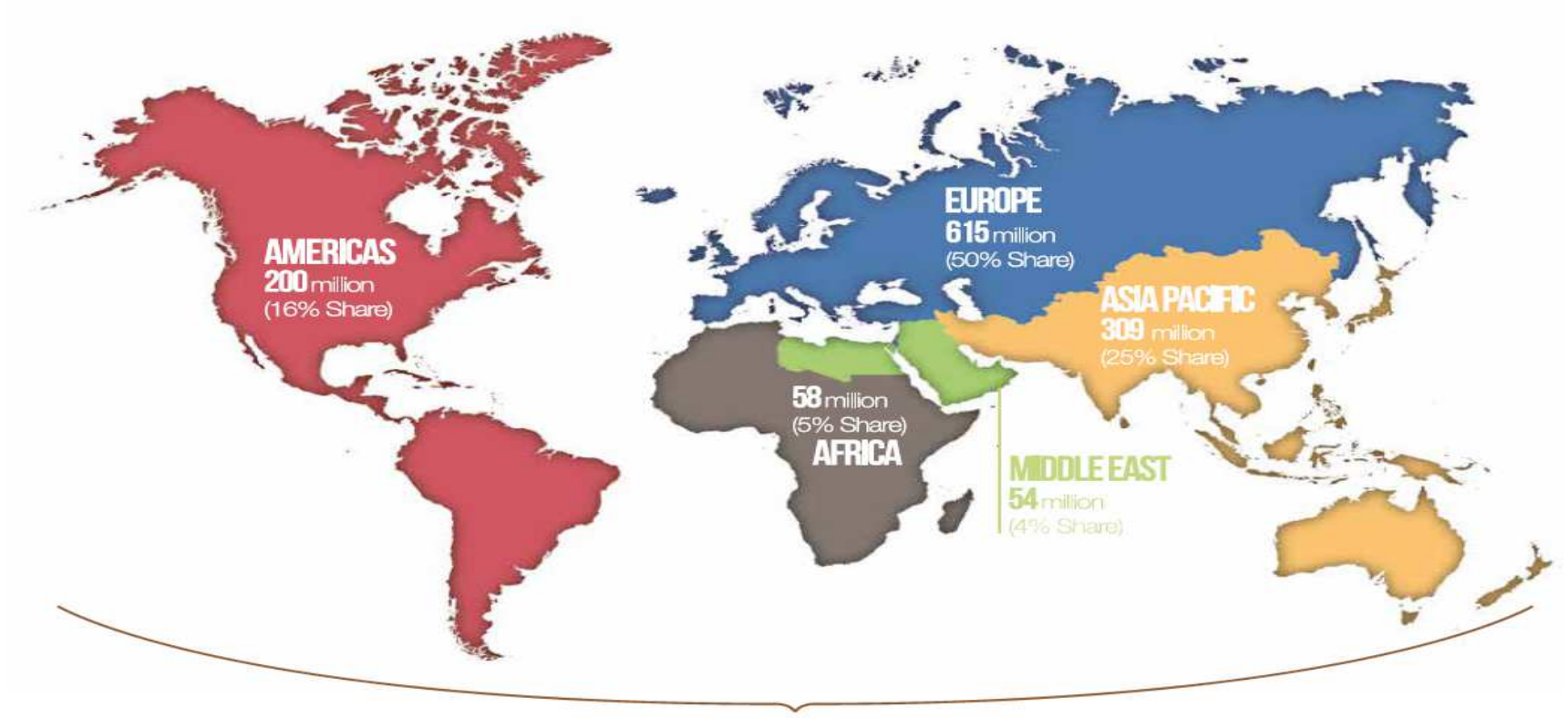
EDICINE

- Introduzione
- Vaccini di routine e per il viaggio
- Esempi dal *portfolio* vaccinale del viaggiatore
- La profilassi antimalarica
- Conclusioni

INTRODUZIONE

EDICINE

INTERNATIONAL TOURIST ARRIVALS 2016



WORLD: 1,235 MILLION

EDICINE

2016 proved to be another excellent year for international tourism despite many challenges. International tourist arrivals grew for the seventh consecutive year to reach 1.2 billion, a sequence of uninterrupted growth not recorded since the 1960s. The strongest growth was recorded in the Africa and Asia and the Pacific regions.

International tourist arrivals reached 1,235 million in 2016.

2016 saw growth in international arrivals of some 46 million, or 4%, over 2015.

Tourism has grown above average, at around 4% per year, for seven straight years.

300 million more people travelled internationally for tourism between 2008 and 2016.

Growth in advanced economy destinations (+5%) exceeded that of emerging economies (+2%) in 2016.

EDICINE

Press Release

2017 International Tourism Results: the highest in seven years

PR No.: 18003
15 Jan 18

International tourist arrivals grew by a remarkable 7% in 2017 to reach a total of 1,322 million, according to the latest UNWTO World Tourism Barometer. This strong momentum is expected to continue in 2018 at a rate of 4%-5%.

Based on data reported by destinations around the world, it is estimated that international tourist arrivals (overnight visitors) worldwide increased 7% in 2017. This is well above the sustained and consistent trend of 4% or higher growth since 2010 and represents the strongest results in seven years.

Led by Mediterranean destinations, Europe recorded extraordinary results for such a large and rather mature region, with 8% more international arrivals than in 2016. Africa consolidated its 2016 rebound with an 8% increase. Asia and the Pacific recorded 6% growth, the Middle East 5% and the Americas 3%.

2017 was characterised by sustained growth in many destinations and a firm recovery in those that suffered decreases in previous years. Results were partly shaped by the global economic upswing and the robust outbound demand from many traditional and emerging source markets, particularly a rebound in tourism spending from Brazil and the Russian Federation after a few years of declines.

"International travel continues to grow strongly, consolidating the tourism sector as a key driver in economic development. As the third export sector in the world, tourism is essential for job creation and the prosperity of communities around the world." said UNWTO Secretary-General Zurab Pololikashvili. "Yet as we continue to grow we must work closer together to ensure this growth benefits every member of every host community, and is in line with the Sustainable Development Goals".

Growth expected to continue in 2018

The current strong momentum is expected to continue in 2018, though at a more sustainable pace after eight years

EDICINE

VACCINI DI ROUTINE

e

PER IL VIAGGIO

DUE PASSAGGI NELLA VACCINAZIONE DEI VIAGGIATOR

EDICINE

Aggiornamento dei vaccini di routine

Offerta di vaccini specifici per il viaggio

DUE PASSAGGI NELLA VACCINAZIONE DEI VIAGGIATOR

EDICINE

- Precedenti vaccinazioni
- Anamnesi

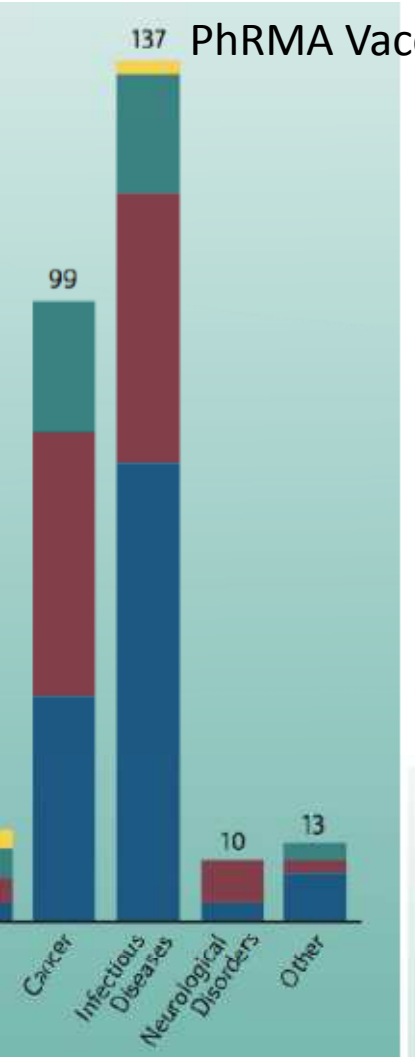
giornamento dei vaccini di routine

erta di vaccini specifici per il viaggio

- Info dettagliate sull'itinerario
- Condizioni di vita in viaggio
- Modo e scopo del viaggio
- Conoscenza delle interazioni dei vaccini
- Preferenze del viaggiatore (costi?)

ESEMPI DAL *PORTFOLIO* VACCINALE DEL VIAGGIATORE

EDICINE



PhRMA Vaccine Factbook 2013

- **FEBBRE GIALLA**
- **RABBIA**
- **DENGUE**

271

Table 14.1 Type of vaccines

Live vaccines	Inactivated vaccines	Toxoid va
BCG	Anthrax	Diphtheria
Measles, mumps, rubella	Cholera (oral, parenteral)	Tetanus
Oral cholera	Haemophilus (Hib)	
Oral poliomyelitis	Hepatitis A	
Oral typhoid	Hepatitis B	
Varicella	Influenza	
Yellow fever	Japanese encephalitis	
	Pertussis	
	Plague	
	Pneumococcus	
	Inactivated poliomyelitis	
	Rabies	
	Tick-borne encephalitis	
	Inactivated typhoid	

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FEBBRE GIALLA

FEBBRE GIALLA

EDICINE

Flavivirus

Febbre emorragica virale trasmessa da nzare (*Aedes* o *Haemagogus* spp*)*

Clinica: da asintomatica a mortale

Distribuzione: spt Africa sub-sahariana, entro e Sud America

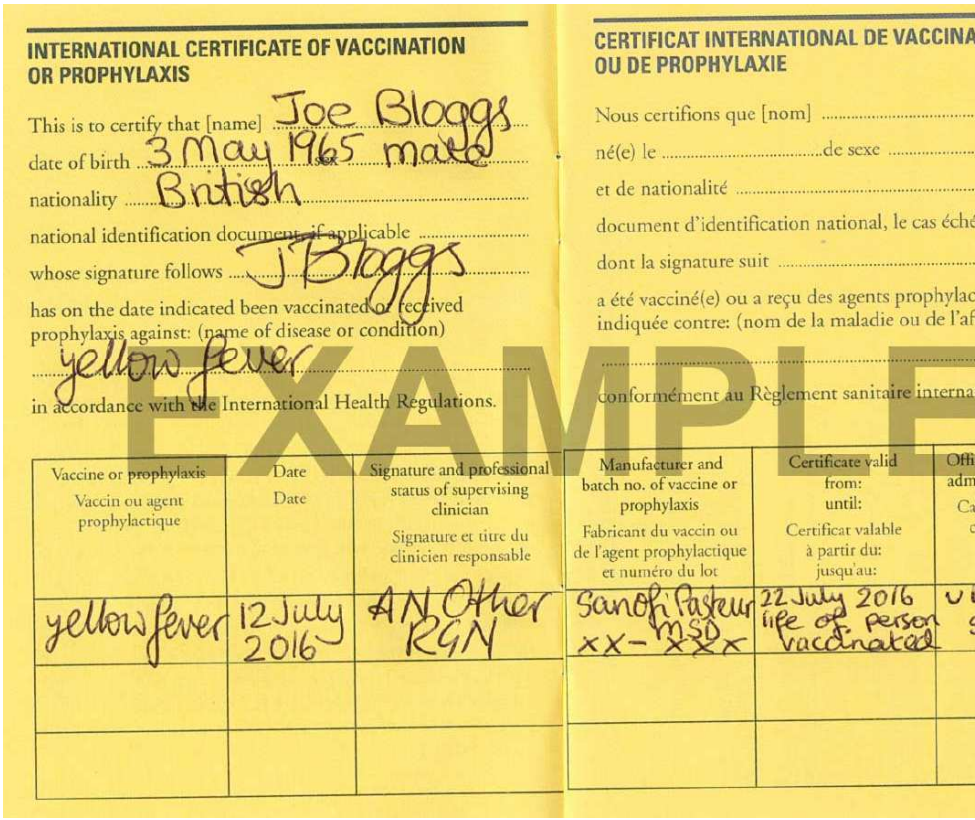
Ripresa della malattia in ambo i continenti colpire popolazione locale e viaggiatori

VACCINO FG

EDICINE

ò essere:

Richiesto per entrare in un
ese, secondo l'International
ealth Regulation (2005)



INTERNATIONAL CERTIFICATE OF VACCINATION OR PROPHYLAXIS

This is to certify that [name] Joe Bloggs
date of birth 3 May 1965 male
nationality British
national identification document, if applicable
whose signature follows J Bloggs
has on the date indicated been vaccinated or received prophylaxis against: (name of disease or condition)
yellow fever
in accordance with the International Health Regulations.

Vaccine or prophylaxis Vaccin ou agent prophylactique	Date Date	Signature and professional status of supervising clinician Signature et titre du clinicien responsable	Manufacturer and batch no. of vaccine or prophylaxis Fabricant du vaccin ou de l'agent prophylactique et numéro du lot	Certificate valid from: until: Certificat valable à partir du: jusqu'au:
yellow fever	12 July 2016	AN Other RGN	Sanofi Pasteur MSD xx-xxx	22 July 2016 life of person vaccinated

CERTIFICAT INTERNATIONAL DE VACCINA OU DE PROPHYLAXIE

Nous certifions que [nom]
né(e) le ..... de sexe
et de nationalité
document d'identification national, le cas éch
dont la signature suit
a été vacciné(e) ou a reçu des agents prophylac indiquée contre: (nom de la maladie ou de l'af
conformément au Règlement sanitaire interna

EXAMPLE

Raccomandato per il rischio durante un viaggio in
ea endemica

VACCINO FO

EDICINE

- Certificato valido da 10 gg dopo la vaccinazione
solo per la 1^ dose)

- Da luglio 2016, il booster a 10 aa è stato rimosso
ed il certificato è valido a vita (retroattivo)

DA DOVE VIENE QUESTA DECISIONE?

EDICINE

WHO. Meeting of the Strategic Advisory Group of Experts (SAGE) on immunization, April 2013 – conclusions and recommendations. *WER* 2013; 88: 201-6.

WHO. Vaccines and vaccination against yellow fever. WHO position paper – June 2013. *WER* 2013; 88: 269-83.

MA...

EDICINE

Staples et al. Yellow fever vaccine booster doses: recommendations of the Advisory Committee on Immunization Practices (ACIP). *CDC MMWR* 2015; 64: 647-50.

accinazione/Booster è raccomandata per:

- **Donne in gravidanza alla 1^ vaccinazione**
- **Riceventi di HSCT dopo YFV**
- **HIV +**
- **Personale di laboratorio che lavora con il virus selvaggio**

e...

• A booster dose may be given to travelers who received their last dose of yellow fever vaccine at least 10 years previously and who will be in a ***higher-risk setting*** based on season, location, activities, and duration of their travel [Category B]. This would include travelers who plan to spend a prolonged period in endemic areas or those traveling to highly endemic areas such as rural West Africa during peak transmission season or an area with an ongoing outbreak.

EDICINE

?

UNCERTAINTY OF LIFE-LONG PROTECTION OF YFV FOR TRAVELLERS

EDICINE

Little evidence for life-long protection after a single dose of YFV

- esp for travellers from non endemic areas

Studies included: majority of vaccinees lived or stayed for a prolonged period of time

- role of natural immunity/natural “booster”

Methods of measuring immune response after YFV differed by studies

Rapid decline was seen in immunocompetent travellers (Niedrig et al., 1999)

Vaccine failure might be underestimated (Camara et al., 2008)

Role of T-cells?

- repetitive stimulation for long-term immune response (Campi-Azevedo et al., 2016)

UNCERTAINTY OF LIFE-LONG PROTECTION OF YFV FOR TRAVELLERS

EDICINE

Little evidence for life-long protection after a single dose of YFV

WHY NOT GIVE A SINGLE BOOSTER?

Role of T-cells?

- repetitive stimulation for long-term immune response (Campi-Azevedo et al., 2016)

EVENTI AVVERSI GRAVI DA VACCINO ANTI-FEBBRE GIALL

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YEL-AND = 0.8/10^5, ma 1.6/10^5 in 60-69 e 2.3/10^5 in >70

Raramente fatale

Molto raramente con dosi booster

YEL-AVD = 0.4/10^5, ma 1.0/10^5 in 60-69 e 2.3/10^5 in >70

≈ 60% mortalità

Mai vista con dosi booster

EDICINE

Immunogenicity of Fractional-Dose Vaccine during a Yellow Fever Outbreak — Preliminary Report

Steve Ahuka-Mundeke, M.D., Ph.D., Rebecca M. Casey, M.B., B.S., M.P.H., Jennifer B. Harris, Ph.D., M.P.H., Meredith G. Dixon, M.D., Pierre M. Nsele, M.D., Gabriel M. Kizito, M.D., Grace Umutesi, M.P.H., Janeen Laven, B.S., Gilson Paluku, M.D., M.P.H., Abdou S. Gueye, M.D., Ph.D., Terri B. Hyde, M.D., M.P.H., Guylain K.M. Sheria, M.D., Ph.D., Jean-Jacques Muyembe-Tanfum, M.D., Ph.D., and J. Erin Staples, M.D., Ph.D.

This article was published on Februa 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1710430

- Vaccination with one-fifth the standard dose of yellow fever (YF) vaccine in an outbrea etting elicited an antibody response in 98% of initially seronegative recipients and a ≥ 4- old increase in geometric mean titer (GMT) of YF neutralizing antibodies in 66% of initia eropositive recipients.

- Fractional doses of YF vaccine may be useful in controlling an outbreak of YF when upplies of vaccine are constrained.

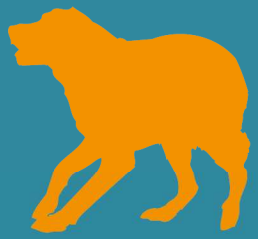
- Fractional doses of YF vaccine are not generally recommended for travelers because uration of efficacy and safety data are still inadequate, and an International Certificate accination or Prophylaxis (ICVP) for YF cannot be issued.

RABBIA

RABIES

Zero deaths by 2030

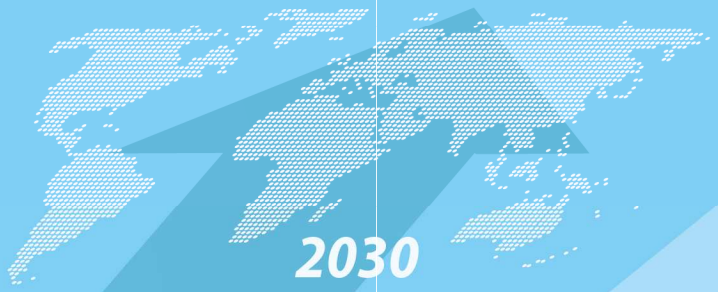
99% human cases result from **dog bites**

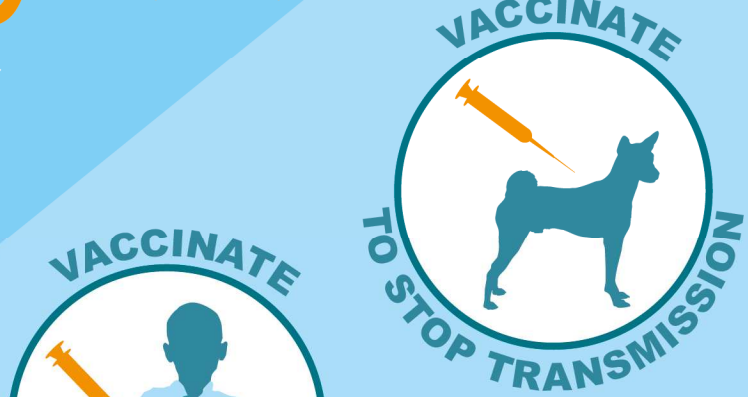


One death

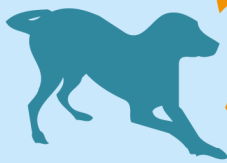
every **15 minutes** worldwide

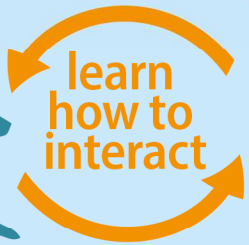
4 out of 10 deaths are in **children**





100% vaccine preventable





no bite
no rabies

World Health Organization

#rabies
28 September
World Rabies Day
www.who.int/rabies/en

EDICINE

Journal of Travel Medicine

International Society of Travel Medicine
Promoting healthy travel worldwide
Established 1991

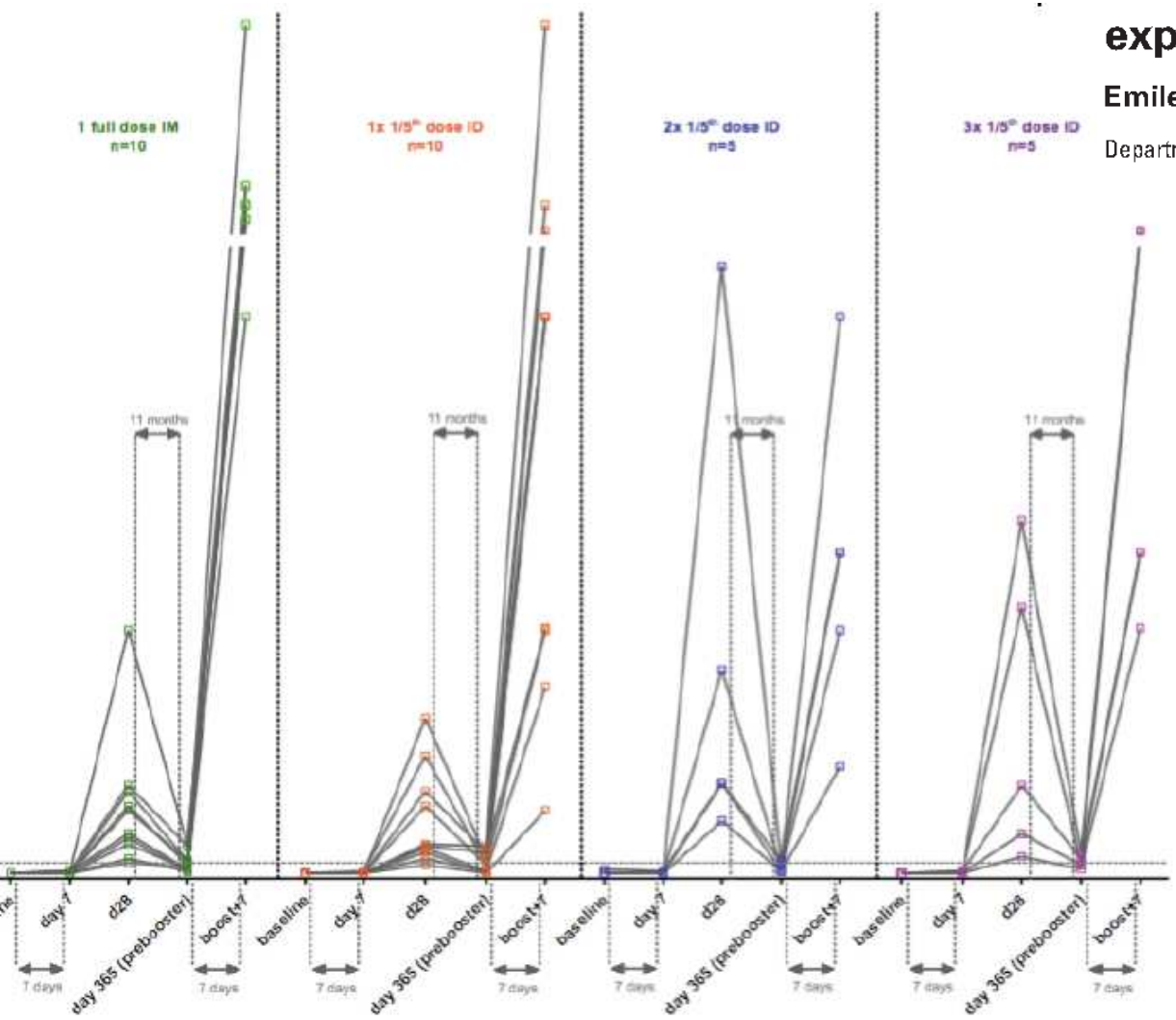
Journal of Travel M
doi: 1

Original article

Single visit rabies pre-exposure priming induces a anamnestic antibody response after simulated pos exposure vaccination: results of a dose-finding stu

Emile F.F. Jonker, MD, and Leonardus G. Visser, MD, PhD*

Department of Infectious Diseases, Leiden University Medical Center (LUMC), Leiden, The Netherlands



EDICINE

WHO Background paper: proposed revision of the polic on rabies vaccines and rabie immunoglobulines

22 Sep 2017

ckground paper 2010

idence and grading

Duration of immunity with cell-culture-based vaccines (CCV):

derate evidence that CCV induces > 10 years immunity

Efficacy of cell-culture-based rabies vaccines:

h evidence that CCV are efficacious and induce antibodies owing IM and ID (three visit: 3IM and 3ID)

Safety of cell-culture-based vaccines:

derate evidence that CCV are safe; however transient local ctions may occur

Background paper Sep 2017

Strategic Advisory Group of Experts (SAGE) + Rabies expert gr

New guideline on Rabies prevention expected early in 2018

World Health Organization

Simplified PrEP Rabies schedules:

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Conventional rabies vaccine schedule

IM 1.0 d 0 - 7 – 28

ID 0.1 d 0 - 7 - 28

Proposed accelerated schedules are considered to be efficacious

ID 0.1 **d 0 - 7 (2-2) ID (double dose)**

moderate evidence: non-inferior to WHO recommended regimens

IM 1.0 **d 0 - 7 (1-1)**

moderate evidence: non-inferior?

Simplified PEP Rabies schedule:

EDICINE

Proposed new accelerated schedules is considered efficacious

without need of HRIG

subject without previous PrEP

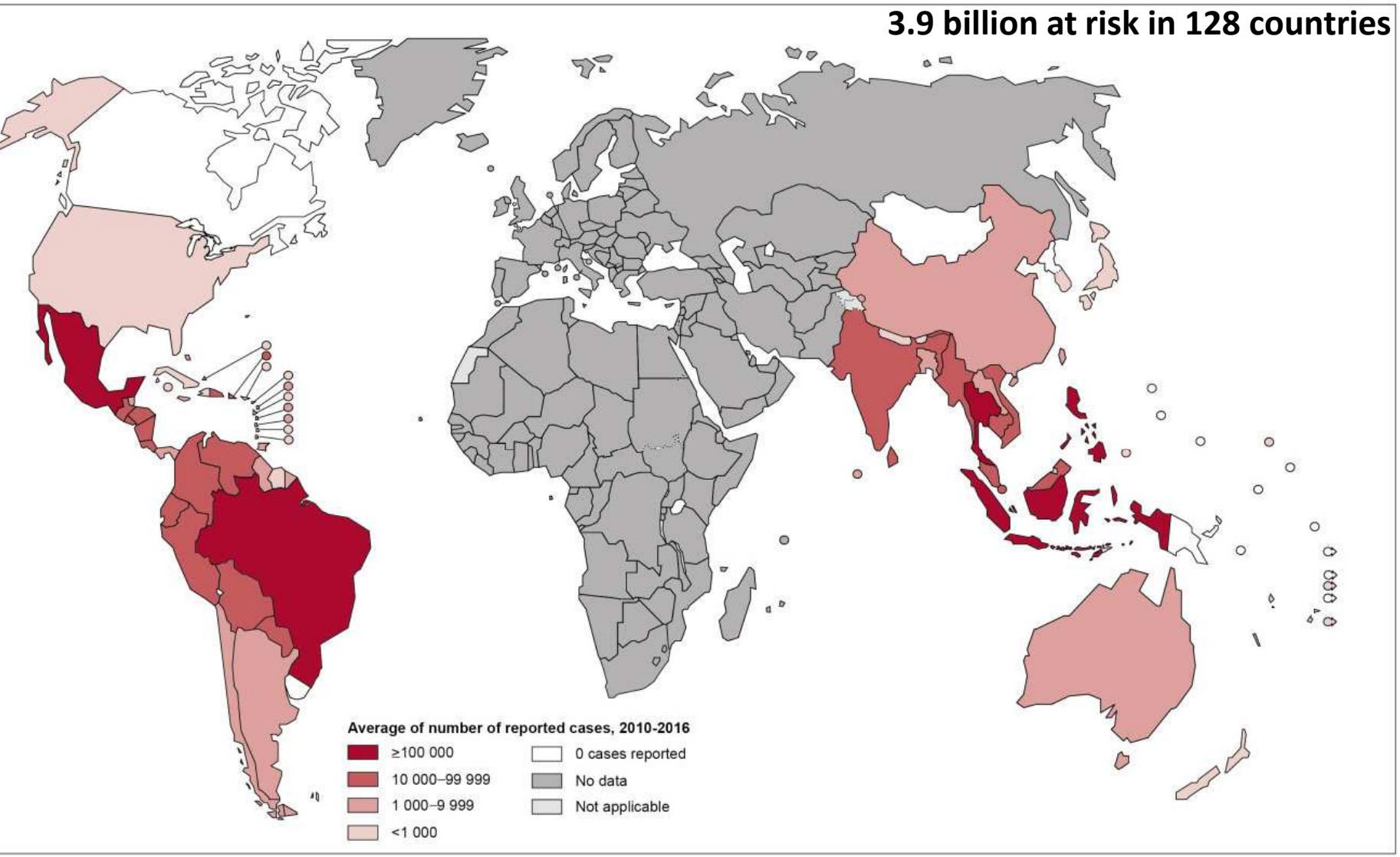
New PEP schedules	Timing	Doses
PEP IPC ID 0.1 without HRIG	d 0 - 3 - 7 " " "	(2-2-2)

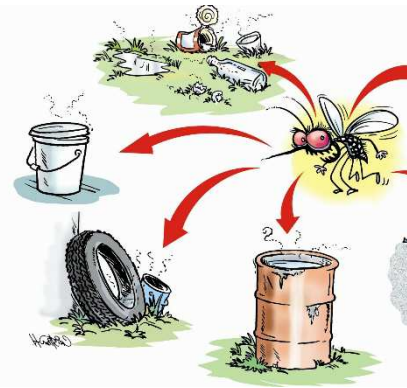
low to moderate evidence on non-inferiority to current WHO recommended regimens

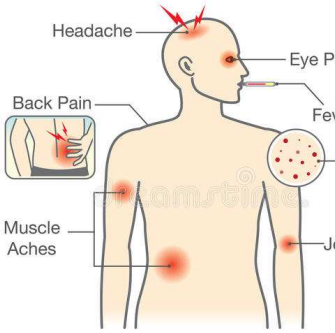
DENGUE

bution of dengue, worldwide, 2016

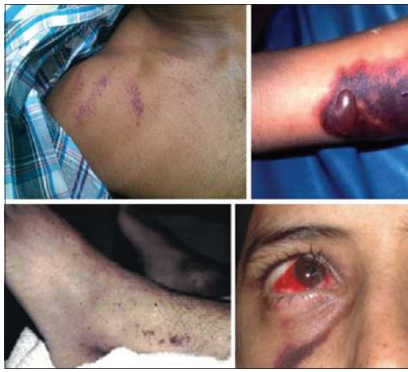
390 M infections/year
100 M any clinical manifestation
3.9 billion at risk in 128 countries







Dengue fever symptoms and



ries and names shown and the designations used on this map do not imply the expression on whatsoever on the part of the World Health Organization concerning the legal status ry, territory, city or area or of its authorities, or concerning the delimitation of its frontiers es. Dotted lines on maps represent approximate border lines for which there may not greement. © WHO 2016. All rights reserved

Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

revious dengue enhancing subsequent infectio

Science

REPORTS

Cite as: L. C. Katzelnick *et al.*, *Science*
10.1126/science.aan6836 (2017).

Antibody-dependent enhancement of severe dengue disease in humans

Leah C. Katzelnick,[1] Lionel Gresh,[2] M. Elizabeth Halloran,[3,4] Juan Carlos Mercado,[5] Guillermina Kuan,[6] Aubree Gordon,[7] Angel Balmaseda,[5] Eva Harris[1]*

[1]Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, USA. [2]Sustainable Sciences Institute, Managua, Nicaragua. [3]Department of Biostatistics, University of Washington, USA. [4]Vaccine and Infectious Disease Institute, Hutchinson Research Center, Seattle, Washington, USA. [5]Laboratorio Nacional de Virología, Centro Nacional de Diagnóstico y Referencia, Ministry of Health, Managua, Nicaragua. [6]Centro de Salud Sócrates Flores Vivas, Ministry of Health, Managua, Nicaragua. [7]Department of Epidemiology, School of Public Health, University of Michigan, USA.

*Corresponding author. Email: eharris@berkeley.edu

For dengue viruses (DENV1-4), a specific range of antibody titer has been shown to enhance viral replication in vitro and severe disease in animal models. Although suspected, such antibody-dependent enhancement (ADE) of severe disease has not been shown to occur in humans. Using multiple statistical approaches to study a long-term pediatric cohort in Nicaragua, we show that risk of severe dengue disease is highest within a narrow range of pre-existing anti-DENV antibody titers. By contrast, we observe protection from all symptomatic dengue disease at high antibody titers. Thus, immune correlates of severe dengue must be evaluated separately from correlates of protection against symptomatic disease. These results have implications for studies of dengue pathogenesis and for vaccine development, because enhancement, not just lack of protection, is of concern.

Philippines halts programme for 'dangerous' dengue fever vaccine given to 730,000 children

Vaccine used in £51.5m immunisation drive can cause severe cases of potentially fatal infection, admits manufacturer

Chris Baynes | Friday 1 December 2017 12:18 GMT | 1 comment

VACCINO ANTI-DENGU

EDICINE

w data conclusively indicate that persons receiving the Tetravalent Dengue Vaccine by Sanofi
teur who had not been infected with dengue virus prior to vaccination have a higher risk of
re severe illness and hospitalization due to dengue compared to unvaccinated persons,
ardless of age

IO now recommends that this specific vaccine only be administered to persons with proven
gue infection prior to vaccination, which effectively precludes most travelers

cludes all endemic individuals who have no access to testing for dengue antibodies

e Tetravalent Dengue Vaccine is approved in approximately 20 dengue-endemic countries;
velers and expatriates should be advised to avoid it unless they have reliable laboratory evidenc
past dengue infection

PROSSIMO CANDIDATO - DENGUE

EDICINE

virus, native DENV-2 + chimeric -1,-3,-4

oses 1 yr apart optimal in dengue-naïve (travelers)

NV serotype-specific antibodies at 18 months for all 4 serotypes

% dengue attack rate in placebo; 1.5% in vaccines

ety issues hard to know at this point

Immunogenicity and safety of one versus two doses of tetravalent dengue vaccine in healthy children aged 2–17 years in Asia and Latin America: 18-month interim data from a phase 2, randomised, placebo-controlled study

Xavier Sáez-Llorens, Vianney Tricou, Delia Yu, Luis Rivera, José Jimeno, Ana Cecilia Villarreal, Epiphany Data, Sonia Mazara, Maria Vargas, Manja Brose, Martina Rauscher, Suely Tuboi, Astrid Borkowski, Derek Wallace

Summary

Background Development of vaccines that are effective against all four dengue virus serotypes (DENV-1–4) in all age groups is important. Here, we present 18-month interim data from an ongoing study undertaken to assess the immunogenicity and safety of Takeda's tetravalent dengue vaccine (TDV) candidate over 48 months in children living in dengue-endemic countries.

Methods We undertook a phase 2, multicentre, randomised, double-blind, placebo-controlled study at three sites in

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PROFILASSI ANTIMALARICA

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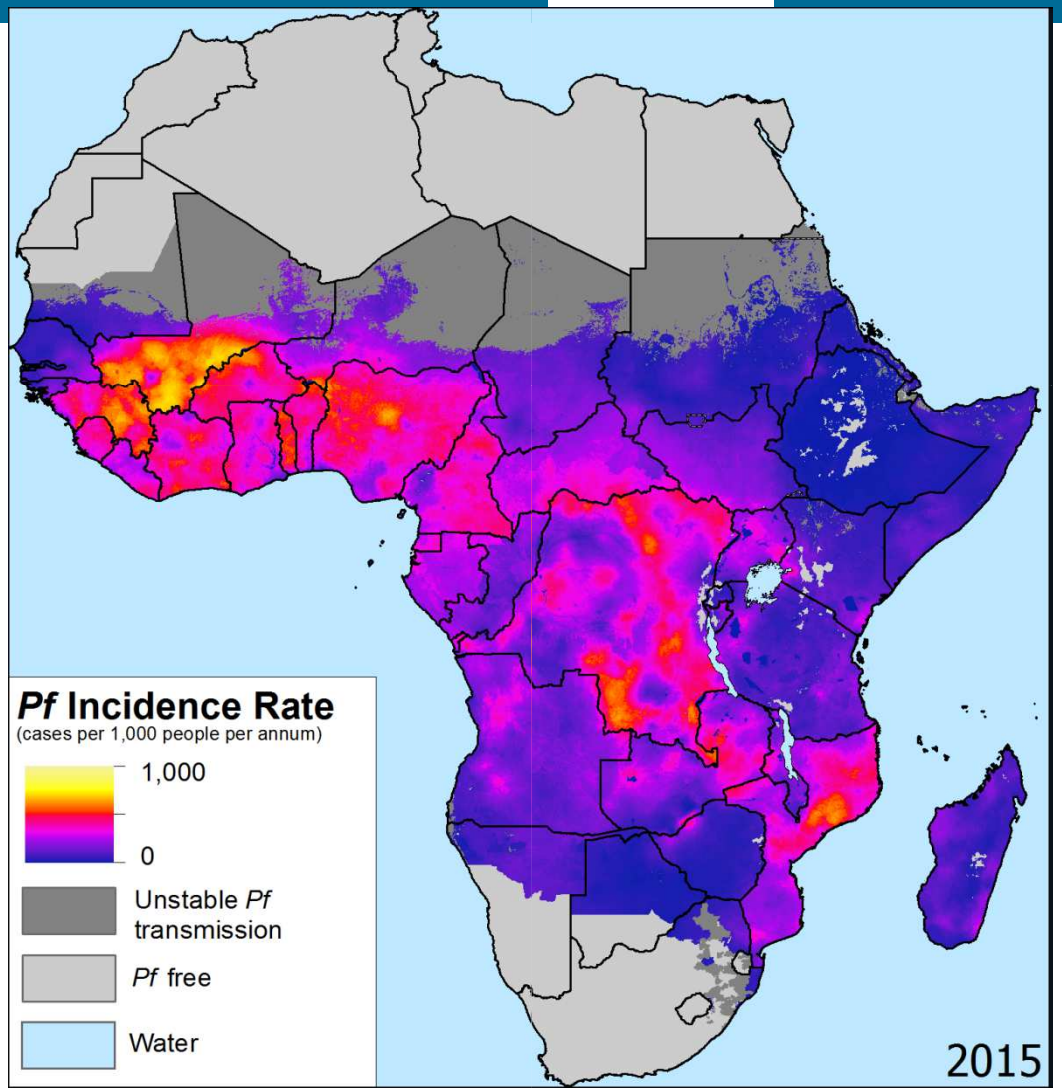
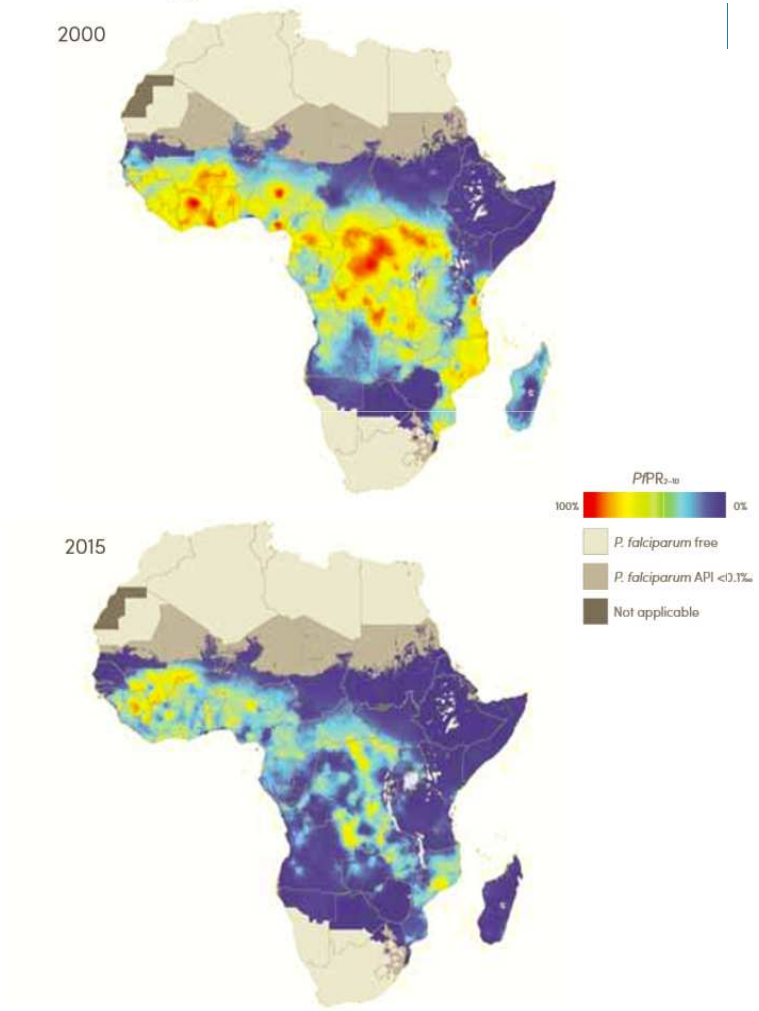

Pf Incidence Rate
(cases per 1,000 people per annum)
1,000
0
Unstable *Pf* transmission
Pf free
Water
2015

EDICINE

2000-2015

Figure 2.5 Estimated *P. falciparum* infection prevalence among children aged 2–10 years ($PfPR_{2-10}$) in 2000 and 2015



API, annual parasite index; *Pf*PR, *P. falciparum* parasite rate
Source: *Malaria Atlas Project (18)*

Malaria morbidity
30% decrease

Malaria mortality
47% decrease

The path to eradication: a progress report on the malaria-eliminating countries

Gretchen Newby, Adam Bennett, Erika Larson, Chris Cotter, Rima Shretta, Allison A Phillips, Richard G A Feachem

In the past several years, as worldwide morbidity and mortality due to malaria have continued to decrease, the global malaria community has grown increasingly supportive of the idea of malaria eradication. In 2015, three noteworthy global documents were released—the WHO's Global Technical Strategy for Malaria 2016–2030, the Roll Back Malaria Partnership's Action and Investment to defeat Malaria 2016–2030, and From Aspiration to Action: What Will It Take to End Malaria?—that collectively advocate for malaria elimination and eradication and outline key operational, technical, and financial strategies to achieve progress toward malaria eradication. In light of this remarkable change in global attitudes toward malaria elimination and eradication, and as the malaria community debates how and when to embark on this ambitious goal, it is important to assess current progress along the path to eradication. Although low-income, high-burden countries are often the focus when discussing the substantial challenges of eradication, the progress toward elimination in middle-income, low-burden countries is a major driver of global progress and deserves better recognition. Additionally, although global support and guidance is essential for success, malaria elimination and eradication efforts will ultimately be driven at the country level and achieved in a collaborative manner, region by region. In this Review, we examine the present status of the 35 malaria-eliminating countries, summarise existing national and regional elimination goals and the regional frameworks that support them, and identify the most crucial enabling factors and potential barriers to achieving eradication by a theoretical end date of 2040.

Lancet 2016; 387: 1775–84

Global Health Group, University of California, San Francisco, San Francisco, CA, USA (G Newby MSPH, A Bennett PhD, E Larson MSc, C Cotter MPH, R Shretta MSc, A A Phillips BA, R G A Feachem DSc[Med])

Correspondence to: Gretchen Newby, University of California, San Francisco Global Health Sciences, Mission Hall, 550 16th Street, San Francisco, CA 94158, USA
gretchen.newby@ucsf.edu

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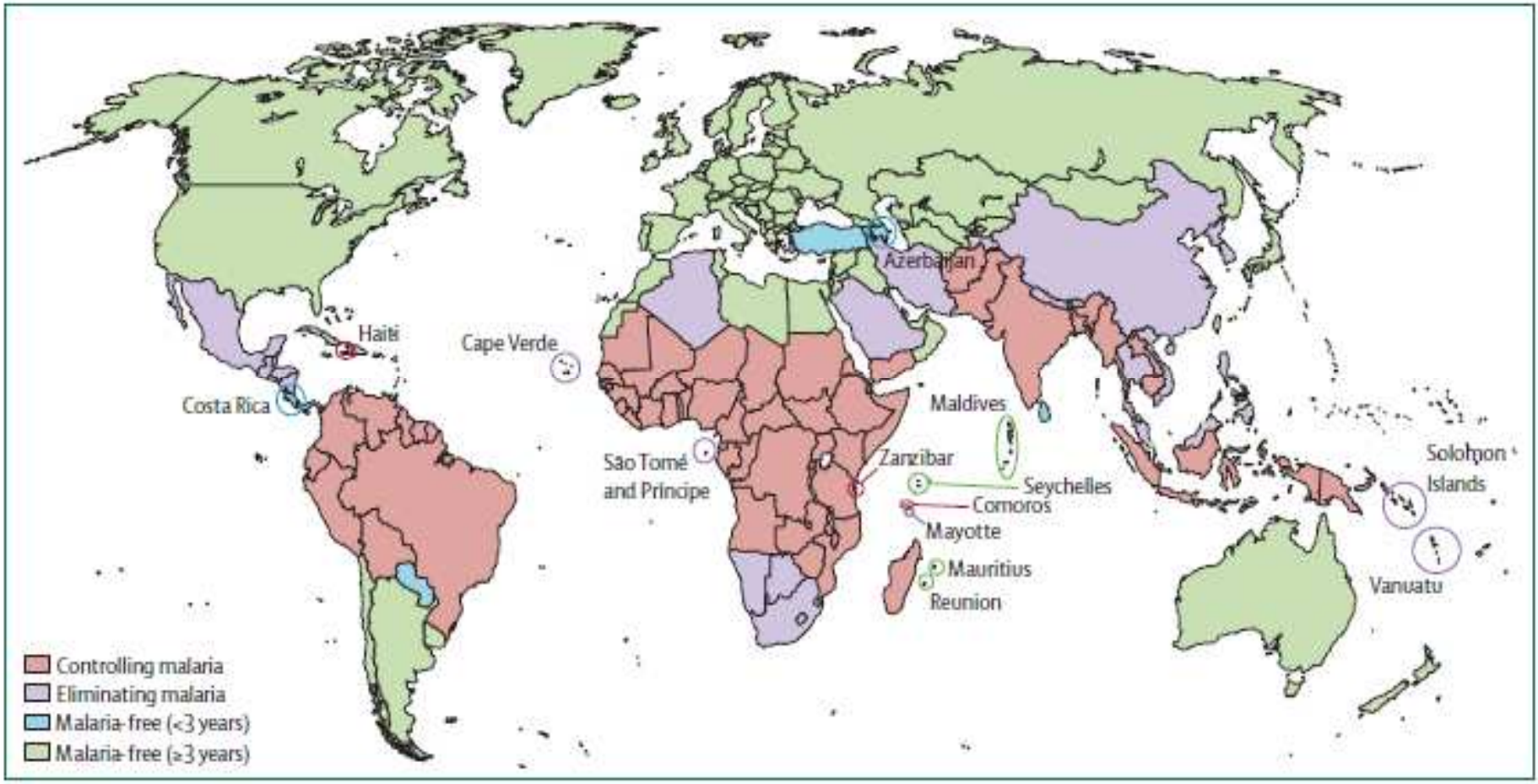

Figure 1: Categorisation of countries as malaria-free, eliminating malaria, or controlling malaria, 2015

The list of eliminating countries is evaluated annually using data collected from WHO's World Malaria Report; national malaria programme reports, elimination strategies, and operational plans; reports and updates from partner organisations and stakeholders; and other resources. When countries are certified by the WHO as malaria-free, or when they report three consecutive years of zero locally transmitted cases in World Malaria Report, they are removed from the eliminating country list. From Shrinking the Malaria Map.

EDICINE

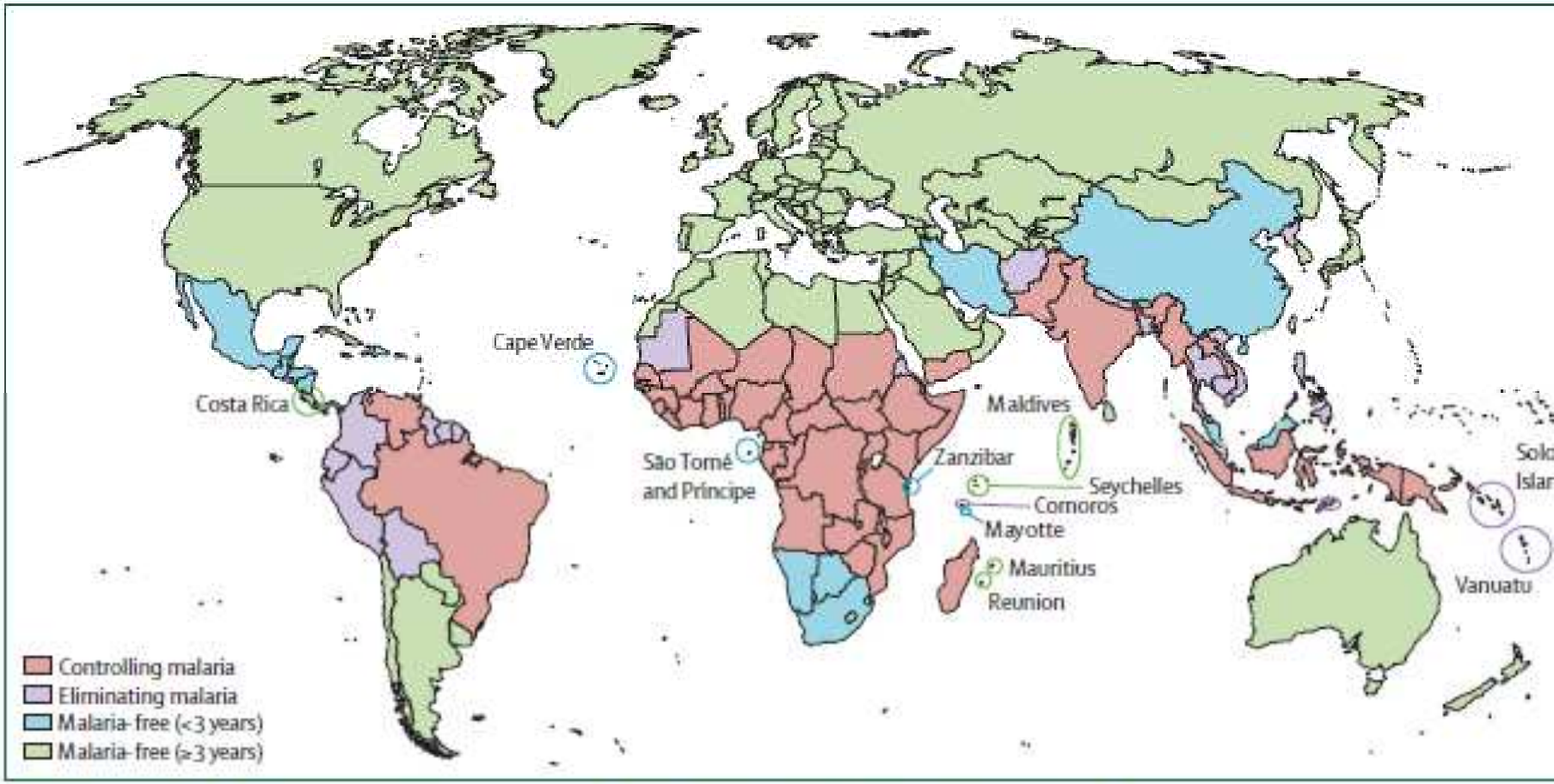

***Figure 4*: Categorisation of countries as malaria-free, eliminating malaria, or controlling malaria, 2020 projection[18]**
Elimination date projections are based on current national and regional goals as well as epidemiological progress as documented in WHO's annual World Malar Report. For those countries that do not currently have clearly defined national or regional goals, elimination dates have been projected based on documented country-level efforts to reach pre-elimination status, recent epidemiological trends, geographical settings such as islands, and the necessary degree of ambition optimism essential to achieve global eradication within a generation.

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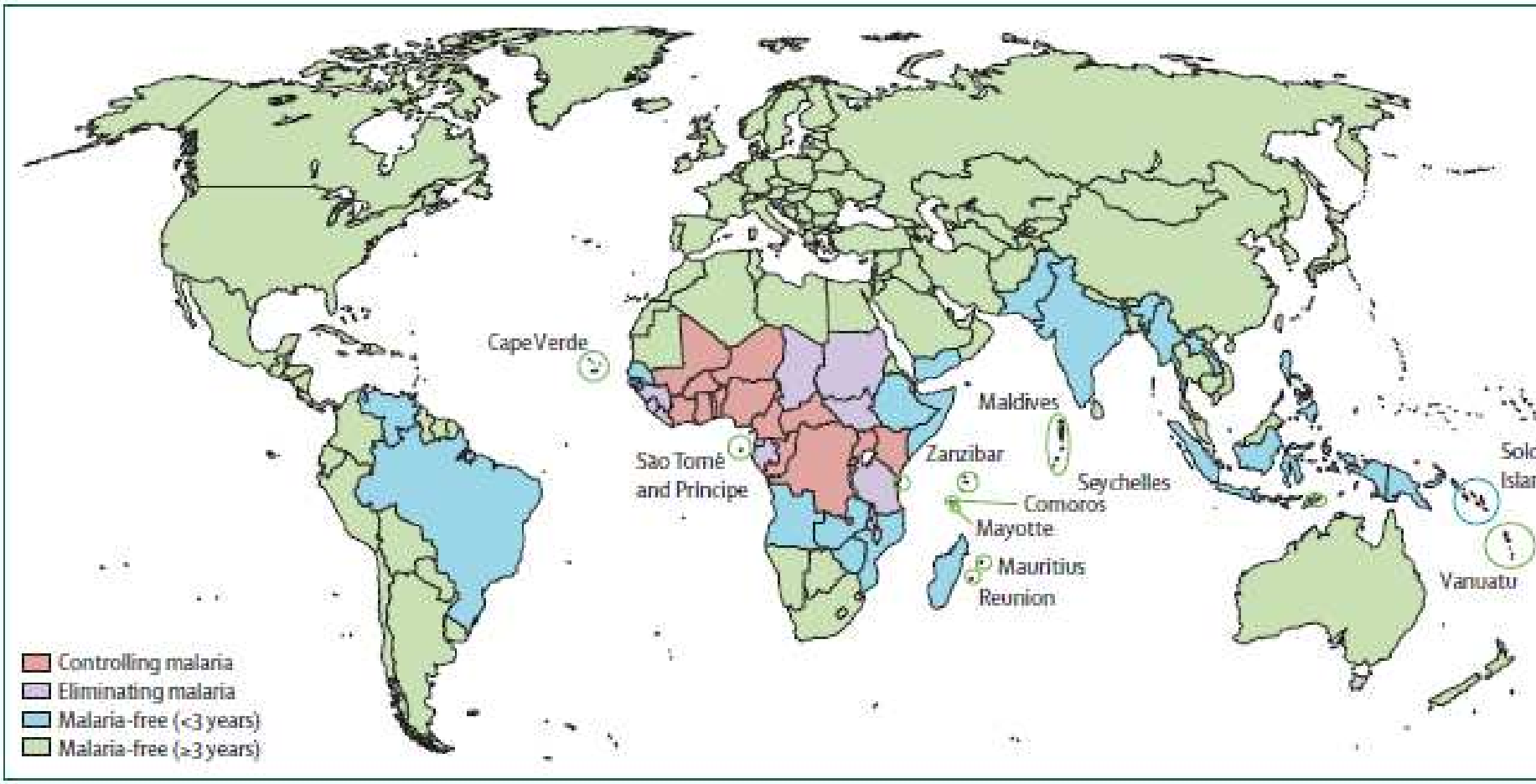


Figure 5: Categorisation of countries as malaria-free, eliminating malaria, or controlling malaria, 2030 projection[69]

Elimination date projections are based on current national and regional goals as well as epidemiological progress as documented in WHO's annual World Malar Report. For those countries that do not currently have clearly defined national or regional goals, elimination dates have been projected based on documented country-level efforts to reach pre-elimination status, recent epidemiological trends, geographical settings such as islands, and the necessary degree of ambitio optimism essential to achieve global eradication within a generation.

Opzioni profilassi 2018

EDICINE

- Atovaquone-proguanil
- Doxiciclina
- Meflochina

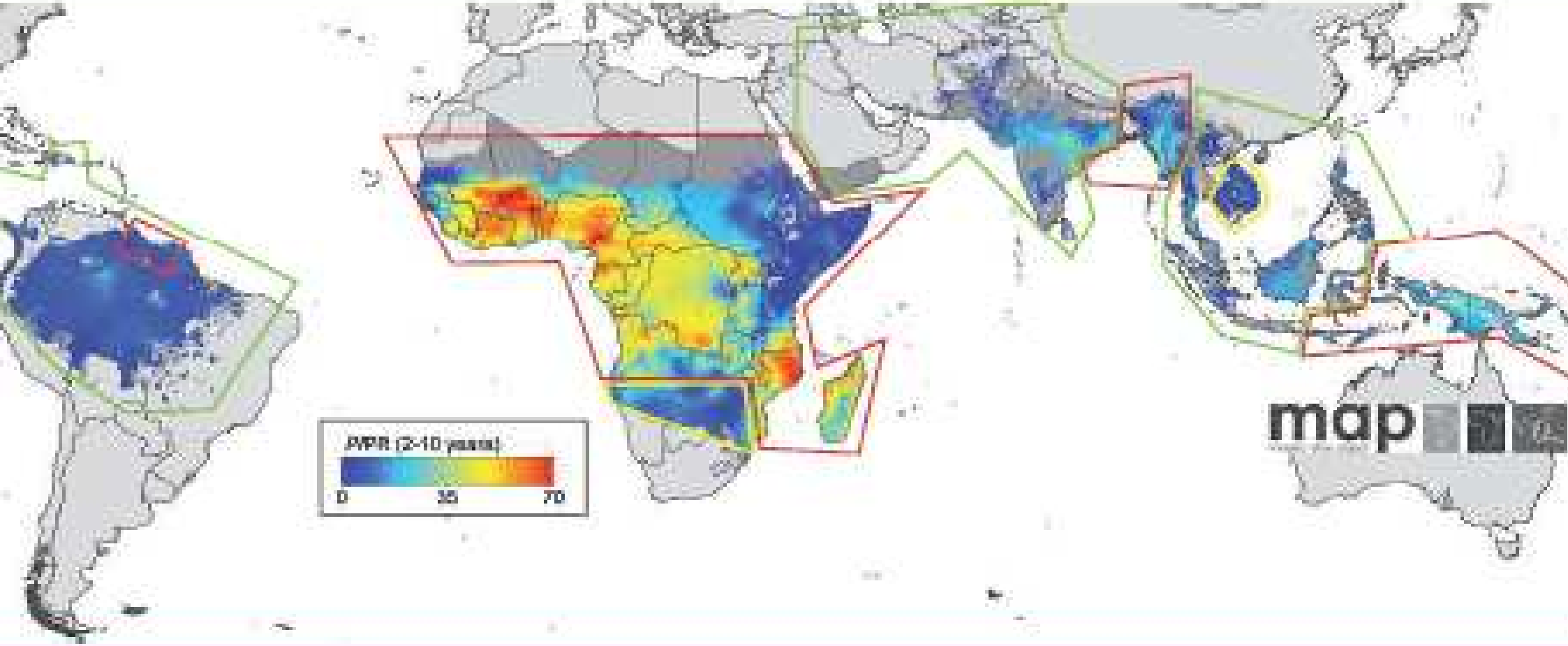
L’ alfabeto della malari

EDICINE

- A wareness
- B ite prevention
- C hemoprophylaxis
- D iagnosis (rapid) & treatment
- E mergency stand-by treatment

Indice 1 — Indicazioni di primo scelta per le profilassi antimalariche secondo le zone geografiche

- Indicata chemioprofilassi
- Indicata chemioprofilassi con alcune limitazioni
- Indicato trattamento presuntivo di emergenza



o da: Gething et al. A new world malaria map: Plasmodium falciparum endemicity in 2010.
arrist 2011, 10:378 http://www.malariajournal.com/content/10/1/378)

EDICINE

tp://www.simetweb.eu/
cument/3967

EDICINE

CONCLUSIONI

PENSARE !!

EDICINE

Considerare sempre alto rischio/basso impatto come pure basso rischio/alto impatto

I vaccini esistono per proteggere sia le popolazioni visitate sia i viaggiatori

Viaggio come opportunità per aggiornare i vaccini di routine

PENSARE DIVERSAMENT

EDICINE

duzione della memoria immunologica con singola do

rrelazione tra tempistica della vaccinazione e
mitato) periodo di esposizione (es rabbia)

tensione degli intervalli tra dosi successive di vaccini

riazione della profilassi antimalarica secondo il varia
ll'epidemiologia


LE VACCINAZIONI PEDIATRIC
E DEGLI ADULTI:
I PIÙ RECENTI AGGIORNAME
GRAZIE
CAGLIARI TH
14 APRILE 2018