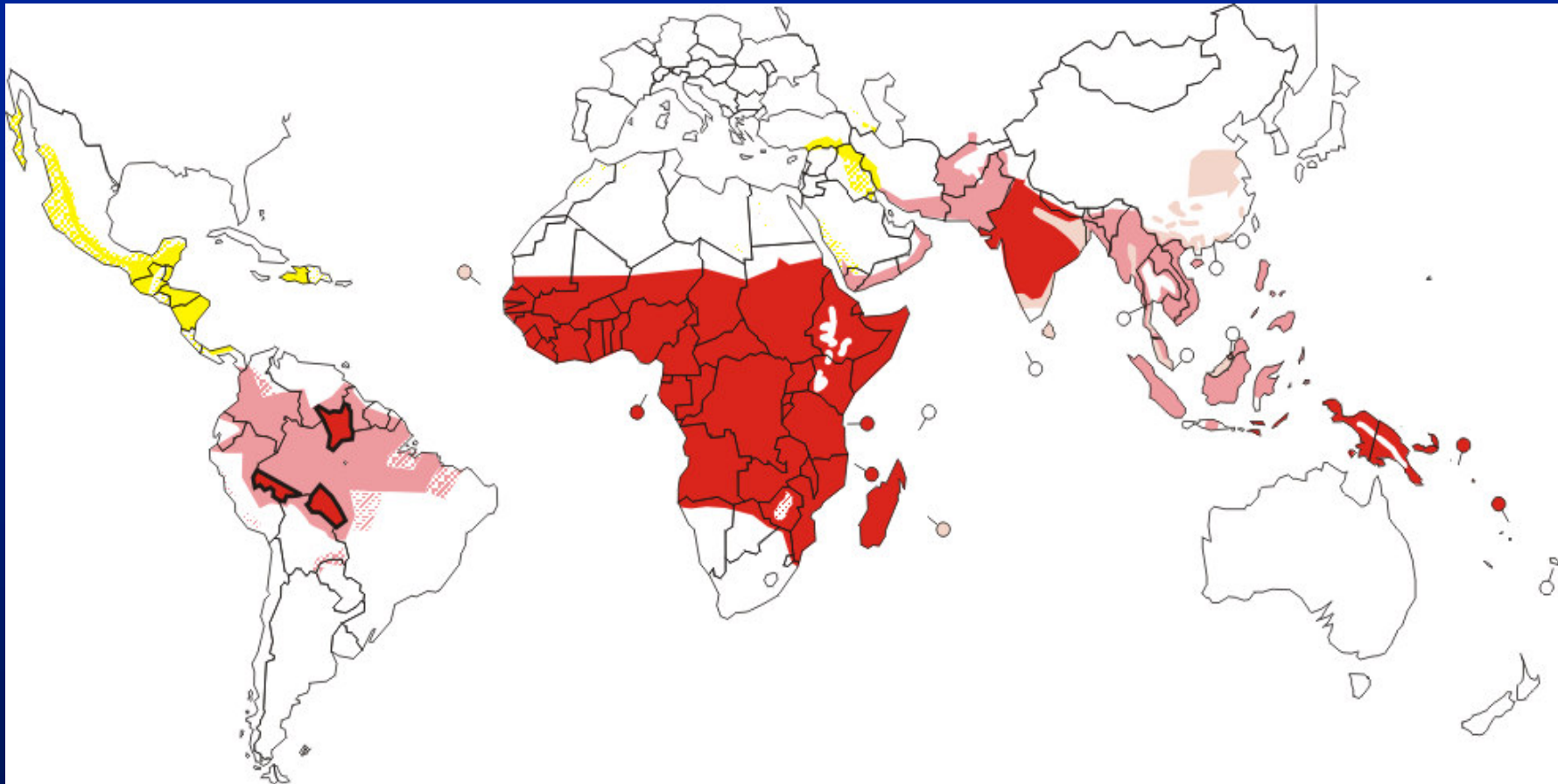


Worldwide malaria risk 2002



Chemoprophylaxis

Stand-by medication

SAR, 2001

Antimalarial strategies: The use of drugs

- Continuous drug intake:
Chemoprophylaxis (=suppression)
- Presumptive treatment in case
of fever: Stand-by medication

Chemoprophylaxis *(=Suppression)*

- In areas with **high** malaria risk
 - Local intensity (e.g. tropical Africa)
 - personal exposure risk
- Resistance problem rather small
- Problem of tolerance and compliance

Duration of drug intake

Check for adverse effects, build up
blood level (1 day-4 weeks)

Suppression of uprising
parasitaemia to avoid severe
disease

Drug intake according to action
and half-life of drugs

Duration of drug intake

Start before departure,
continue during entire stay in
malarious area,
take drug 4 weeks (Malarone® 1
week) after leaving the endemic
area

Presumptive treatment in case of fever: Stand-by medication

- In areas with **low (or moderate)** malaria risk
 - Local scarcity (e.g. many places in SE Asia)
 - personal exposure risk
- **Aim: Prevention of severe disease**
- Tolerance
- Always check with MD in endemic area

Malaria morbidity: estimated attack rate in travellers without chemoprophylaxis

Salomon Isl., PNG	> 3%*	Chemo- prophylaxis
West Africa	2.4%	
East Africa	1.2%	
India	0.35%	
<hr/>		
SE Asia	0.1%	Stand-by medication
Latin America:	0.05%	

* Estimated figure, high proportion of *P. vivax*

Malaria prophylaxis with drugs

Brand name

Generic name

- Lariam[®], Mephaquin[®] Mefloquine
- Supracyclin[®]a.o. Doxycycline
- Nivaquine[®] plus Chloroquine plus
Paludrine[®] Proguanil
- Malarone[®]* Atovaquone plus
Proguanil*

* Registered for prophylactic use in Europe and the US

Adverse effects of Lariam[®]/ Mephaquine[®] in Chemoprophylaxis

- 75% of all travellers have **no or minor** disturbances of well being
- 12% disturbed daily activities
- 1-3% **severe** adverse effects

Malarone[®] for chemoprophylaxis

PRO

- Safety
- Efficacy 98%
- Duration of intake (2 days before until 7 days after travel)
- All age groups
- HIV-positive indiv.

CONTRA

- Unknown rare AE (?)
- Price (Swiss Franks 65.30 for 12 tbl.)
- Unknown interactions (?)
- Pregnancy (?)
- Gastrointestinal AE
- Pressure of media

Outlook



- Mefloquine will be replaced at mid-term in travel medicine by **other drugs**, but keeps a position in combination therapy.
- **Exposure prophylaxis** remains key part of prevention
- Simple malaria prophylaxis with short term intake of **Tafenoquin**?

Which drugs for malaria
treatment?

*Treatment recommendation for tertian
and quartan malaria , and for sensitive
falciparum malaria*

- **Choloroquine**

Primaquine: Eradication of liver forms (in *P. vivax* and *P. ovale*) infections

Treatment recommendation for uncomplicated falciparum malaria

- Mefloquine (Lariam®), Mephaquin®)
- Artemether/Lumefantrin (Riamet)
- Atovaquone/Proguanil (Malarone®)
- Quinine plus doxycycline or clindamycin
- Sulfadoxin/pyrimethamine (Fansidar®) (not for travellers)

Malaria resistance to drugs *(P.falciparum)*

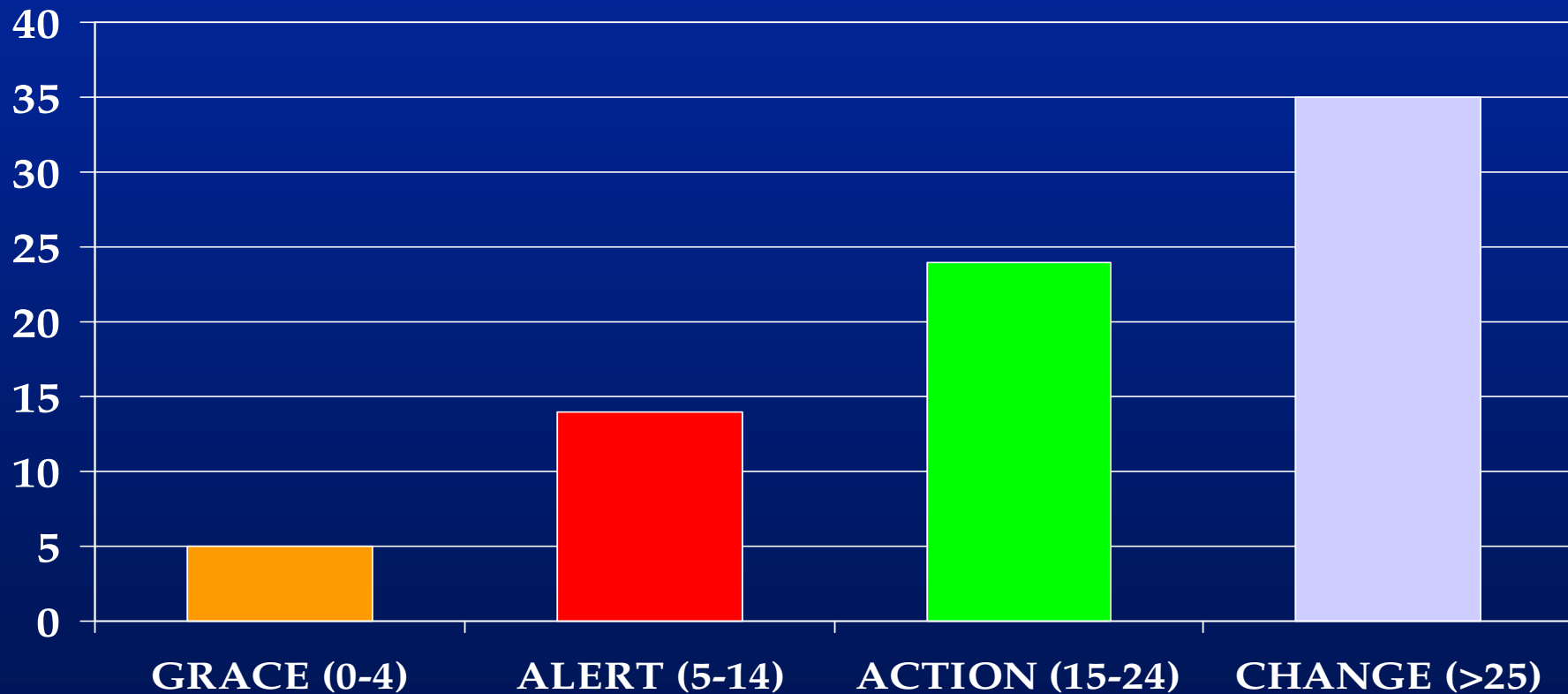
- Chloroquine
 - Worldwide resistance except for Central America and North Africa
- Pyrimethamine/Sulfadoxine
 - Widespread resistance in Asia and South America, increasing in Africa
- Mefloquine and Halofantrine
 - $\geq 50\%$ resistance along borders of Thailand

Factors of drug resistance
development govern the
useful therapeutic life
of an antimalarial drug

White, 1999

Antimalarial drug policy

Steps towards change of first-line drug



Kitua, 1999

What to do?

Combination therapy!

How?

What is available?

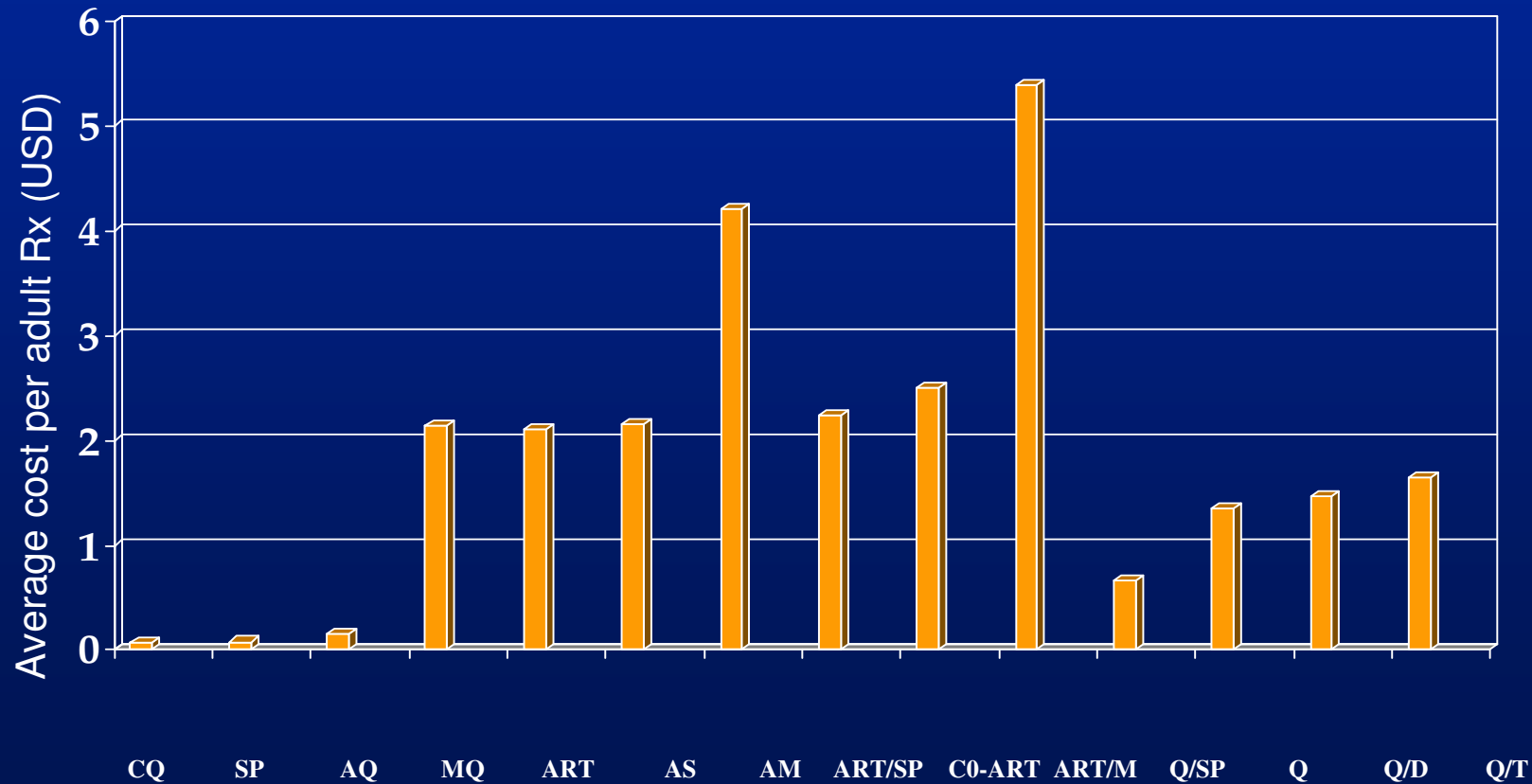
Combination therapy containing artemisinin derivatives

- Artemether / Lumefantrine
- Artesunate / Mefloquine
- Artesunate / Sulfadoxine / Pyrimthamine
- Artesunate / Lapudrine / Dapsone
- Artesunate / Doxycycline

Marketed fixed combination TM

Cost Implications of Antimalaria therapy

Increasingly complex drug regimens



de Savigny, pers. comm.

Global malaria strategy

- Prevent mortality
- Reduce morbidity
- Decrease social and economic loss

Provide early diagnosis and prompt treatment

Perspectives



- Effective treatment with single compounds or even single dose combination regimens are unlikely to be feasible with presently available antimalarial drugs in Africa
- Innovative combinations of longer and shorter (artemisinin) acting compounds for short treatments are warranted