

Artesunate Mefloquine (AsMq)

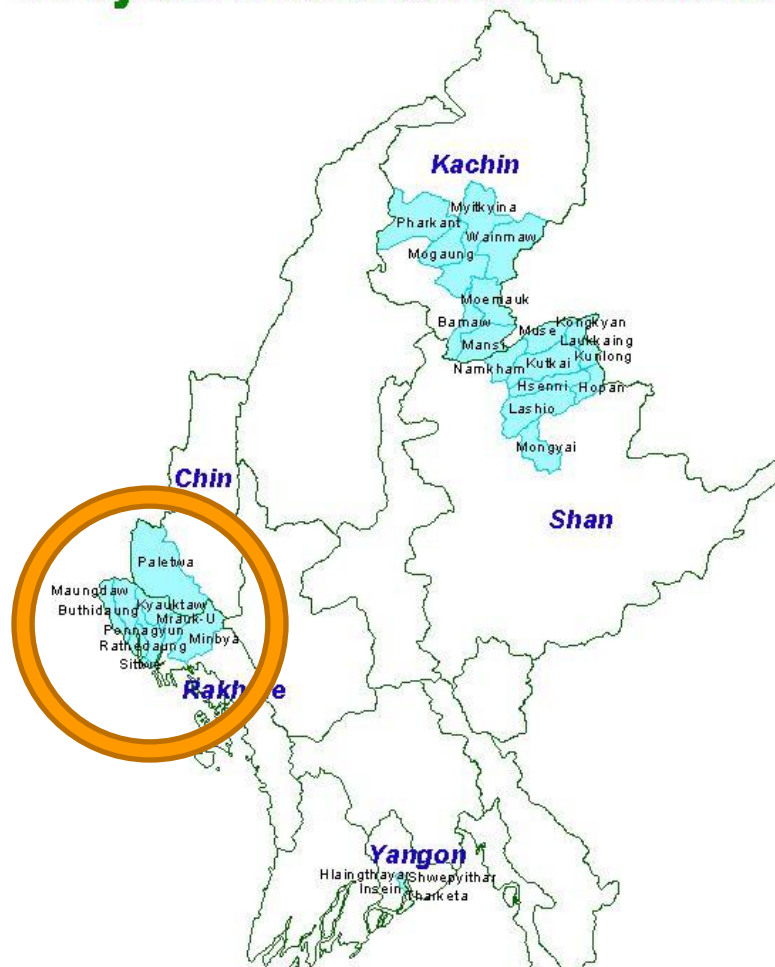
- Introduction AsMq in Rakhine in 1996**
- AsMq FDC compared to other ACTs**

AZG (MSF-Holland) malaria activities in Western Myanmar

9 townships

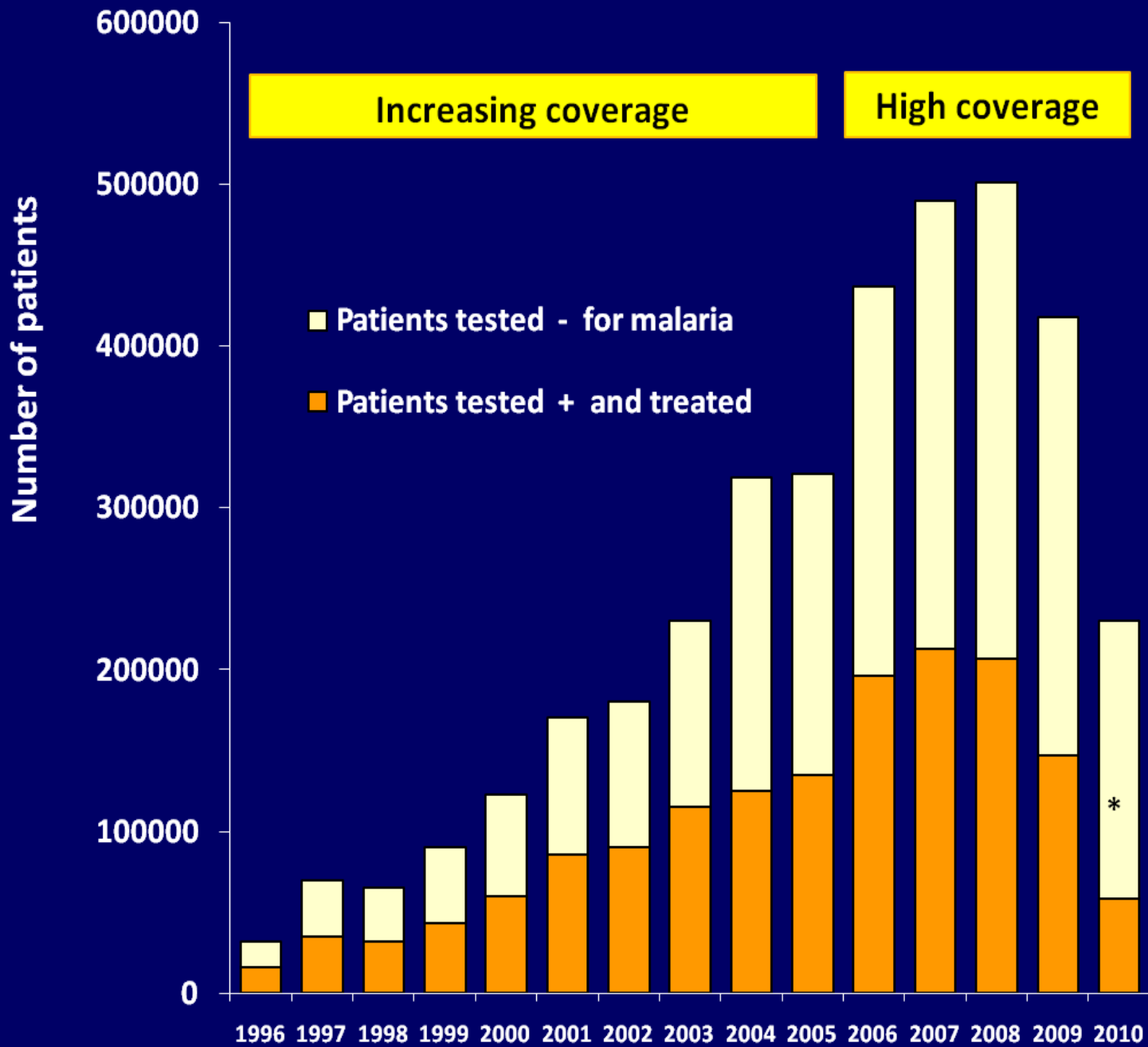
- **25 DoH clinics with AZG support (area 10,000 km²)**
- **Training microscopists, unlimited medicine supply**
- **A small fee (0.15 USD) as incentive for staff**
- **Introduced AsMq for children (1996) and for adults (2001)**

Project Sites Of MSF-Holland



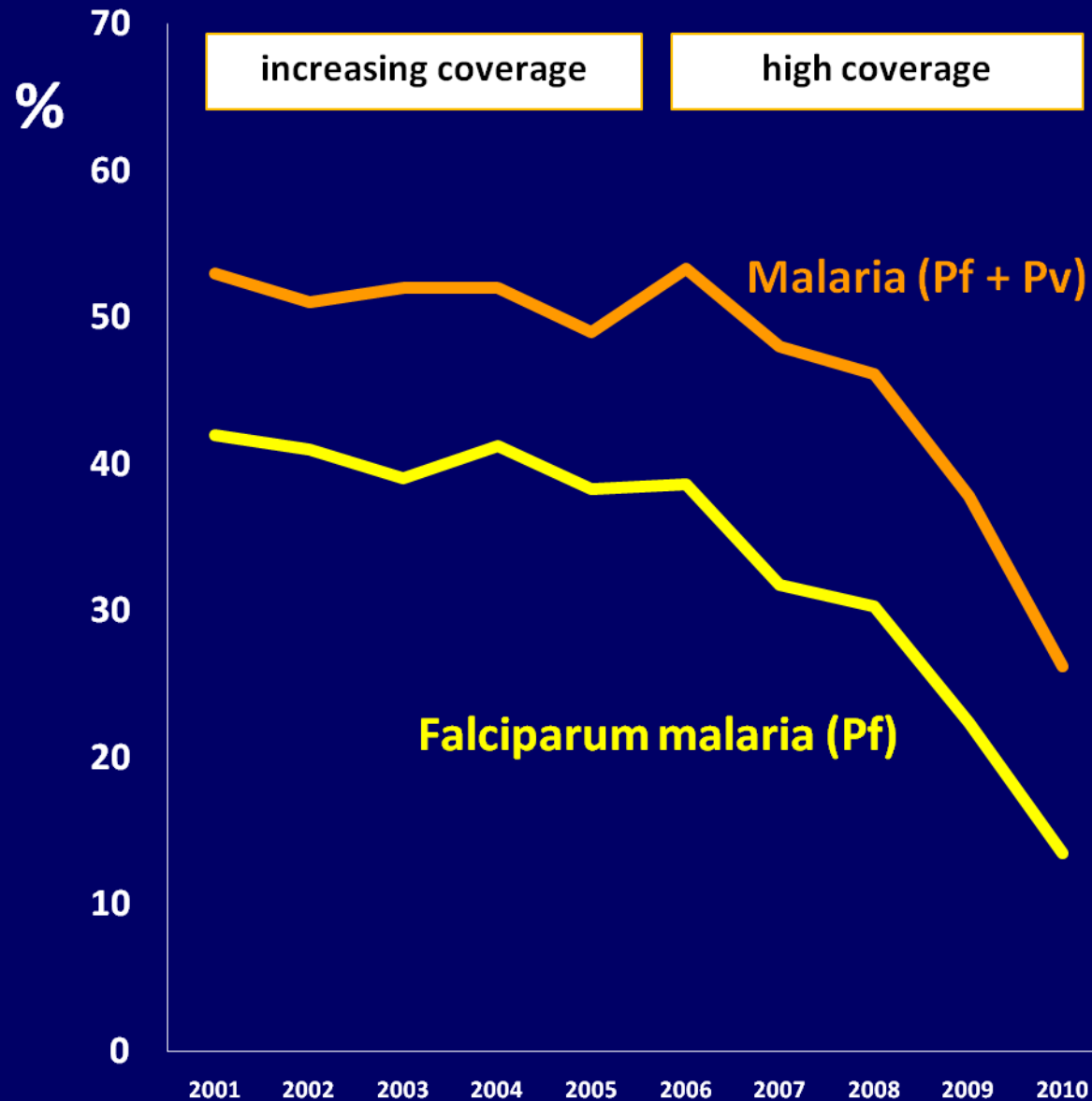
Project Sites





* Data only Jan -Aug

Slide positivity rate, Rakhine project



Conclusion 1

The project was popular.

> 3.5 million tested, > 1.5 million people treated.

2008 survey in 17 villages (<10 km of project clinics);

- 94% of people who had malaria in past year were treated by the project clinics (high coverage)
- “affordable and good”

2009 survey GPs and drug sellers

“Malaria business down”

Conclusion 2

2001 - 2006; more patients, coverage increasing.

→ Modest decrease falciparum positivity rate

2007 - 2010; patient number stabilized, high coverage,

→ Rapid decrease falciparum malaria [from 39% to 14%]

Study

**Comparing the effectiveness of 5
artemisinin combination treatments
in Rakhine, Kachin and Northern Shan**

Effectiveness study; treatment not observed

- Effectiveness on Pf recrudescences and new infections
- Effect on gametocytes
- Effect on P.vivax
- Side effects

10 treatment combinations studied

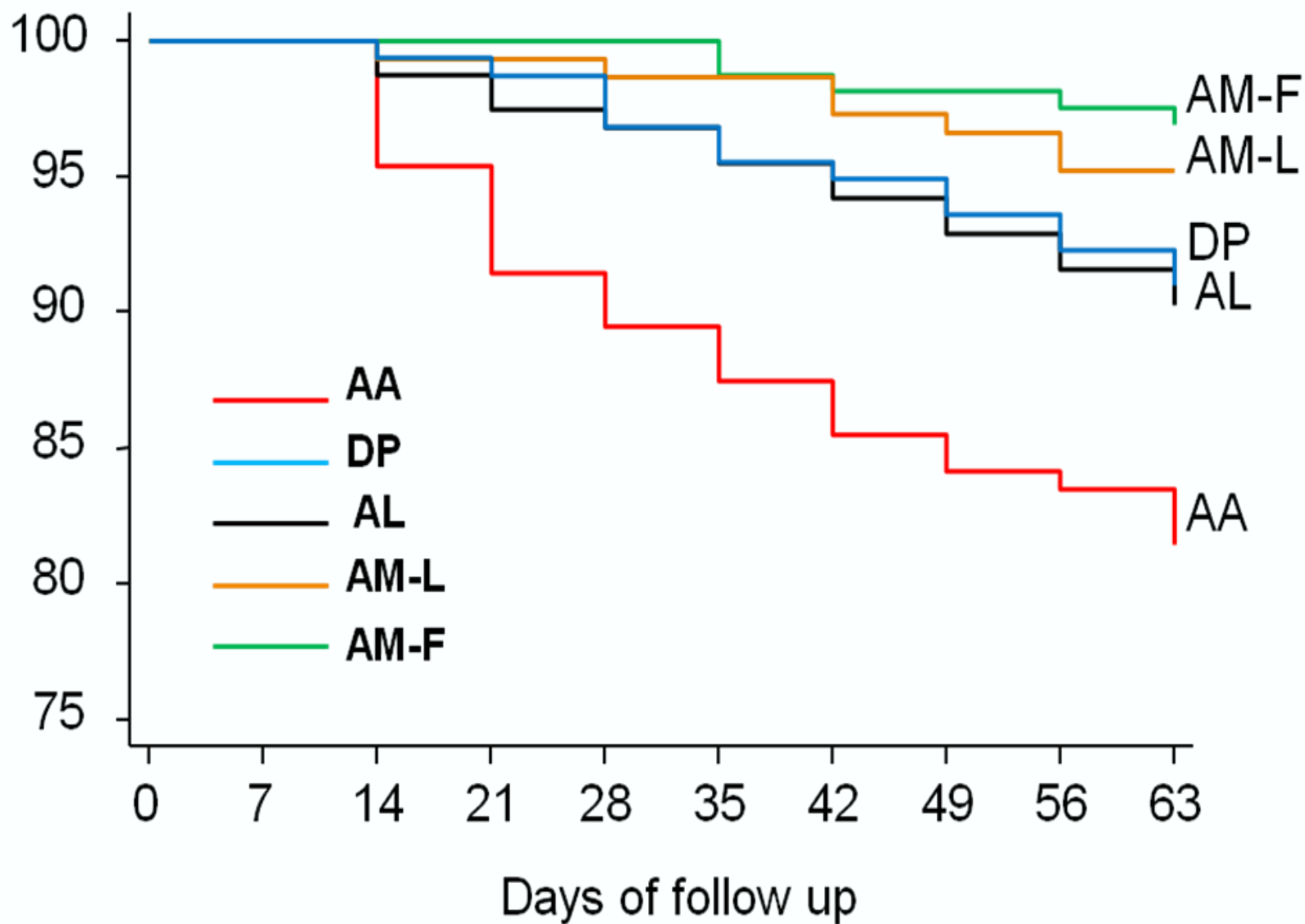
1. AA Artesunate-amodiaquine FDC
2. AL Artemether-lumefantrine FDC
3. AMF Artesunate-mefloquine FDC
4. AML Artesunate-mefloquine loose tablets
5. DP Dihydroartemisinin-piperaquine FDC

With and without primaquine 0.75 mg/kg (SD).

Sample size ; 800

Effect on *P. falciparum*

Patients free of recurrent falciparum malaria (%)



Recurrent *P.falciparum*

Significantly more recurrent Pf after

AA (28) [p<0.0001]

AL (15) [p=0.01]

DP (14) [p=0.02]

than after AMF (5)

Recurrent *P.falciparum*

Defined by DNA study (PCR)

- A recrudescent infection (treatment failure)
- A new infection
- “indeterminate” (no PCR result)

PCR results recurrent *P.falciparum*

69 Pf recurrences

- **38 new inf. (11 AA, 10 AL, 9 DP, 3 AML, 5 AMF)**
- **20 recrudesc. (14 AA, 2 AL, 2 DP, 2 AML, 0 AMF)**
- **11 not defined (3 AA, 3 AL, 3 DP, 2 AML, 0 AMF)**

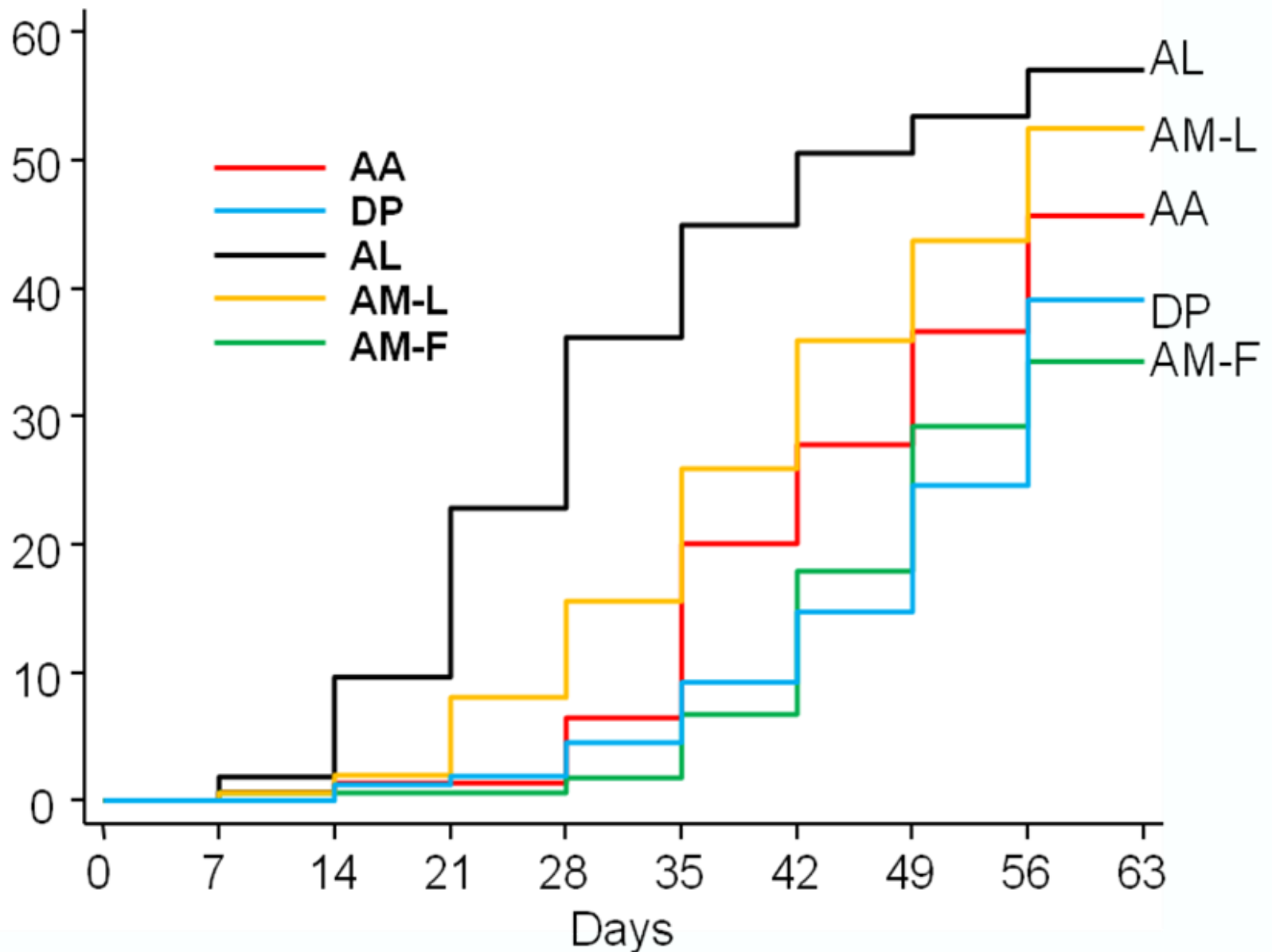
PCR confirmed Pf recrudescences (+ indeterminate PCR)

• Tx	Failures	Fail %	p values *
• AA	14 (17)	9.4 (11.3)	< 0.0001
• AL	2 (5)	1.4 (3.4)	0.14 (0.02)
• DP	2 (5)	1.3 (3.3)	0.14 (0.02)
• AML	2 (4)	1.3 (2.7)	0.14 (0.04)
• AMF	0 (0)	0 (0)	

* *Compared to AsMq FDC*

Effect on vivax malaria

Cumulative *P. vivax* appearance (%)



Vivax appearance compared to AM-FDC

ACT	% vivax by day 63	P value
AM-FDC	34%	
AA	46%	0.02
AL	57%	< 0.0001
AM-LT	53%	< 0.0001
DP	39%	0.7

Effect on gametocytaemia and
transmission

Gametocytaemia

- Artemisinin reduces young gametocytes
- Primaquine reduces adult gametocytes

- Artemisinin + Primaquine ?



Effect on gametocytes

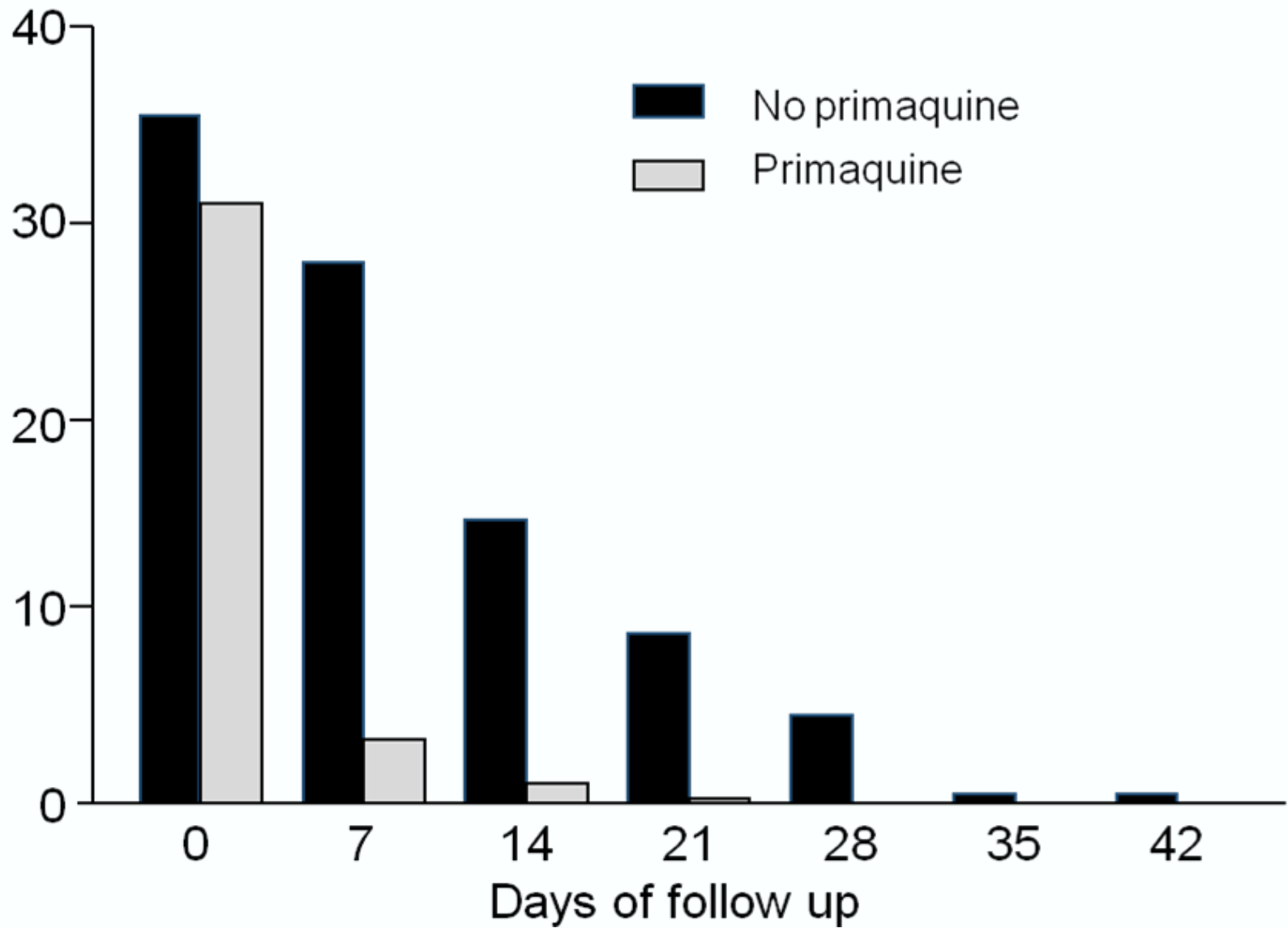
person-gametocyte-time (weeks/1000 weeks follow up)

1. The 5 regimen had different PGTs

<u>Tx</u>	<u>PGT</u>	<u>P value</u>
AA	94	<0.001
AL	58	0.009
AMF	29	
AML	35	0.6
DP	113	<0.001

2. When primaquine was added the 5 ACTs had similar PGTs. [average 5.5]

Patients with gametocytaemia (%)

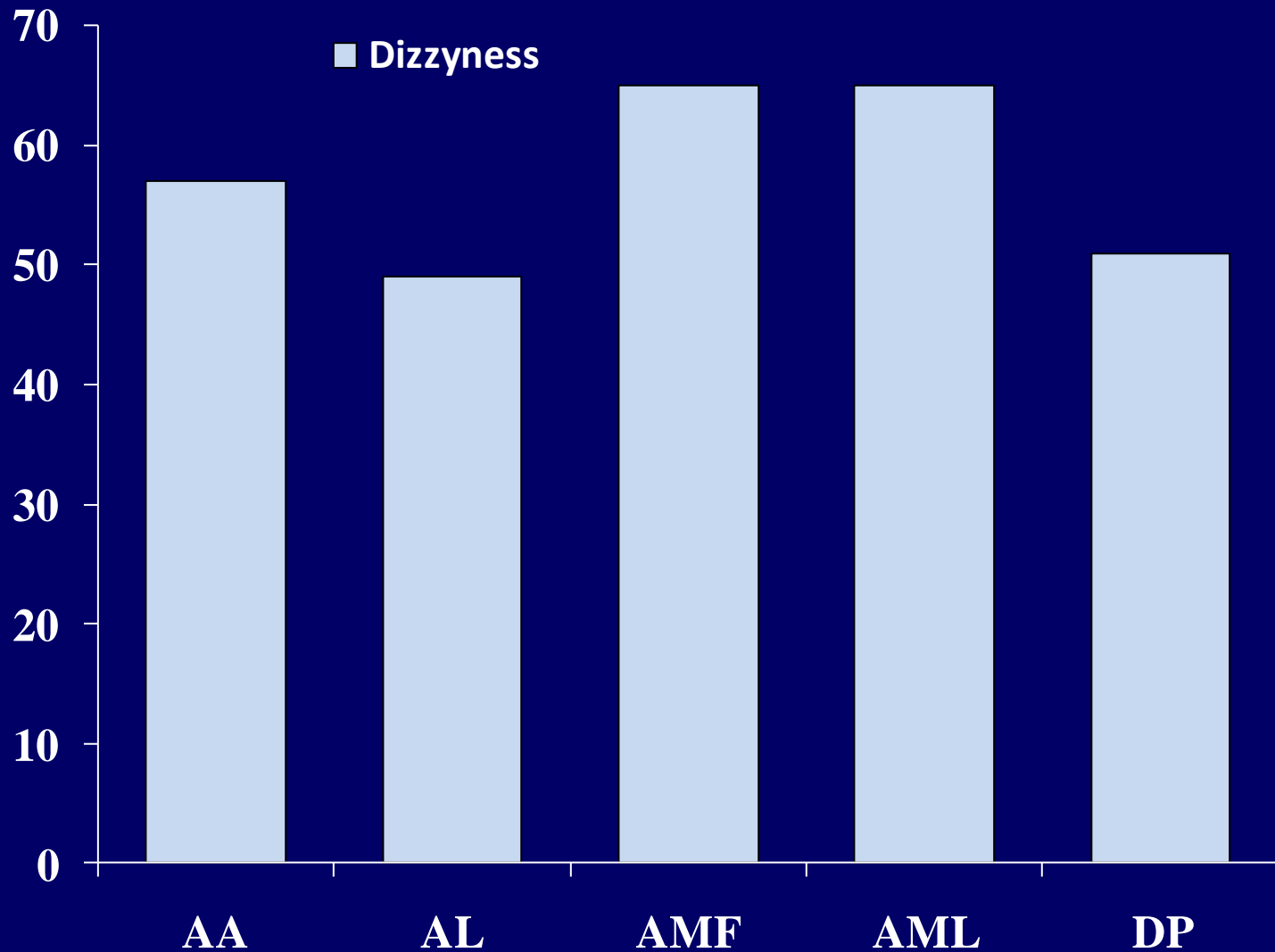


With **ACT plus primaquine**

gametocyte carriage was reduced by a factor **12**

compared to **ACT alone**

Side effects



More dizziness after AM than after AL (RR 1.24, $p=0.03$) and DP (RR 1.22, $p=0.0$)

Haemolysis after primaquine ?

- >400 patients with PQ, no severe haemolysis
- But the mean increase of haemoglobin after primaquine 0.75 g/dL vs 1,04 g/dL (p=0.04)
- *Note*; 14 days primaquine after P vivax has been protocol for many years and no reports of severe haemolysis

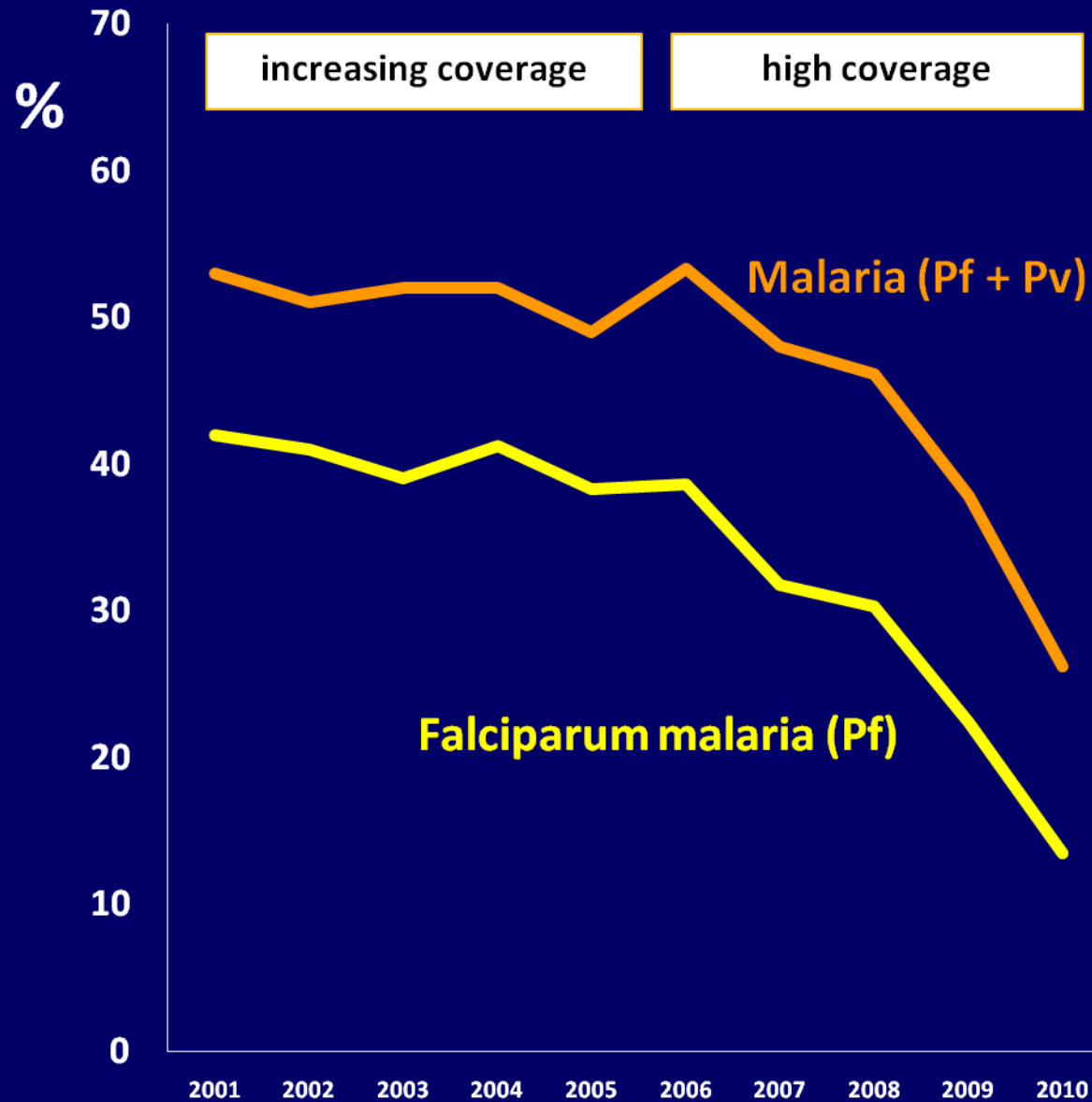
Summary

- AM, DP and AL are all effective for treatment uncomplicated falciparum malaria
- AM FDC had no recrudescence and
 - Less new infections with *P.falciparum*
 - Least *P.vivax* episodes after treatment
 - Least gametocyte-weeks after treatment
 - More dizziness ...
 - 15 years after introduction

Summary 2

- ACT can significantly reduce falciparum malaria if introduced on a large scale
- The addition of a single dose of primaquine has a major effect on malaria transmission and can have a crucial role in elimination programmes

Slide positivity rate Rakhine project



Thank you

