



IN VIVO EFFICACY AND *IN-VITRO* SENSITIVITY
OF ARTESUNATE AND MEFLOROQUINE
DURING 12 YEARS
OF CONTINUOUS DEPLOYMENT
ON THE THAI-MYANMAR BORDER

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Thai-Myanmar border situation



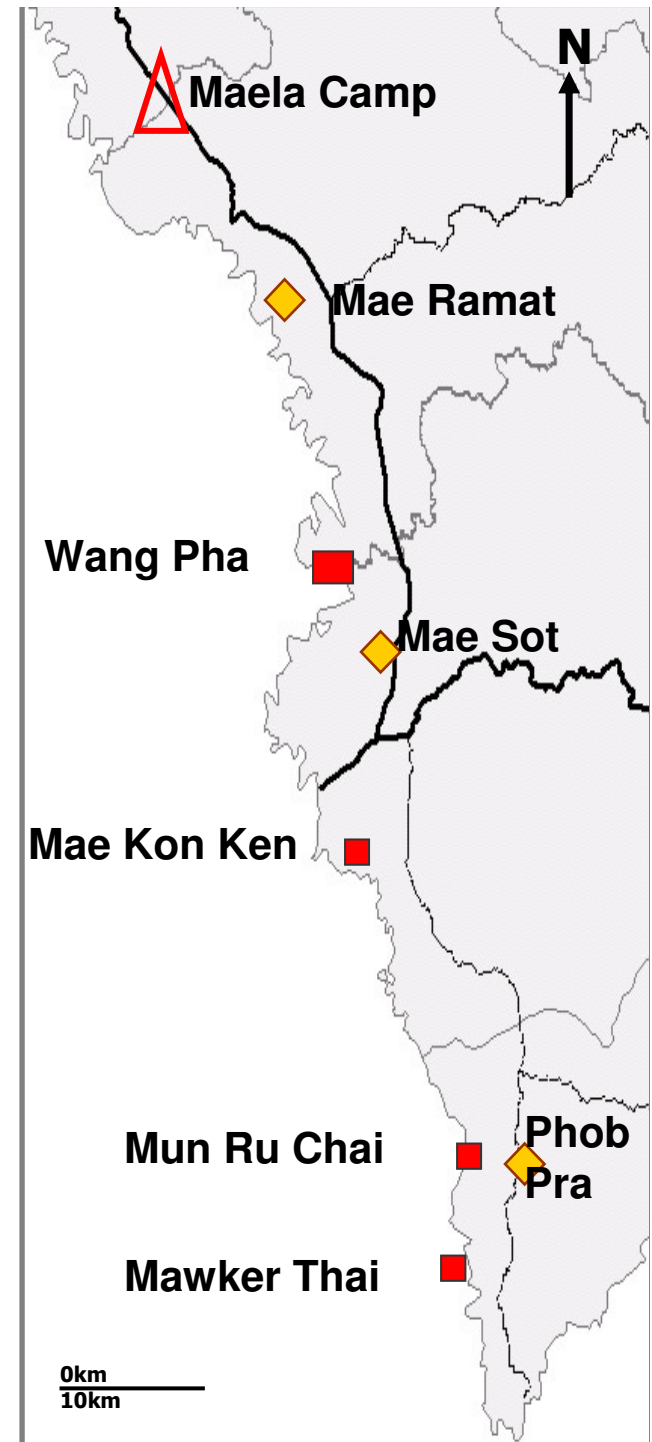
- Complete or partial resistance to all antimalarials except the artemisinin derivatives
- 2-day MAS since 1995 in Tak Province
- 3-day MAS since 1995 in displaced population



MAS₃ in SMRU settings

Monitoring since 1995:

- Parasite clearance time
- PCR-adjusted parasitological efficacy at Day 42
- *In-vitro* susceptibility of Artesunate and Mefloquine
- Molecular markers *pfmdr1* copy number



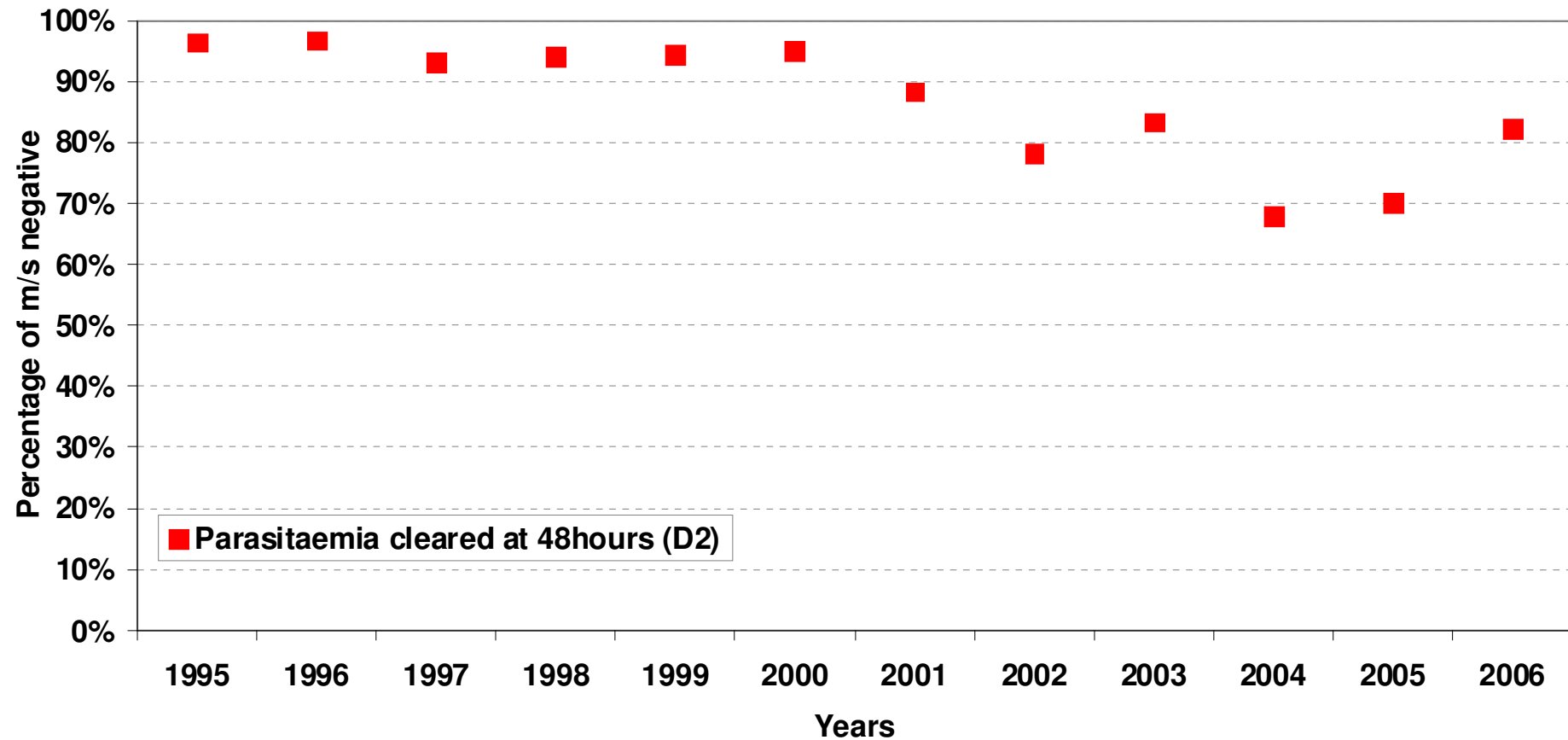
Results

- 3,119 patients enrolled in drug trials between 1995 and 2006
- 66% males
- 1,155 children < 15 years (37%)
- 91% *P. falciparum* mono-infection on admission
- 18% (n=563) patients lost before Day 42 follow-up

Parasite clearance (in table 1995-2006)

<i>Smear positive</i> (N %)	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	Total
Day 0 (admission)	468 (100)	273 (100)	29 (100)	168 (100)	279 (100)	98 (100)	402 (100)	211 (100)	252 (100)	337 (100)	394 (100)	175 (100)	3086 (100)
Day 1	189 (40.4)	106 (38.8)	20 (69.0)	96 (57.1)	150 (53.8)	53 (54.1)	274 (68.2)	159 (75.4)	201 (79.8)	276 (81.9)	320 (81.2)	117 (66.9)	1961 (63.5)
Day 2	17 (3.6)	9 (3.3)	2 (6.9)	10 (6.0)	16 (5.7)	5 (5.1)	47 (11.7)	46 (21.8)	42 (16.7)	108 (32.0)	118 (29.9)	31 (17.7)	451 (14.6)
Day 3	0	0	0	1 (0.6)	1 (0.4)	0	8 (2.0)	8 (3.8)	13 (5.2)	19 (5.6)	26 (6.6)	3 (1.7)	79 (2.6)
Day 4	0	0	0	0	0	0	2 (0.5)	1 (0.5)	1 (0.4)	7 (2.1)	1 (0.3)	1 (0.6)	13 (0.4)
Day 5	0	0	0	0	0	0	0	0	0	1 (0.3)	1 (0.3)	0	2 (0.1)

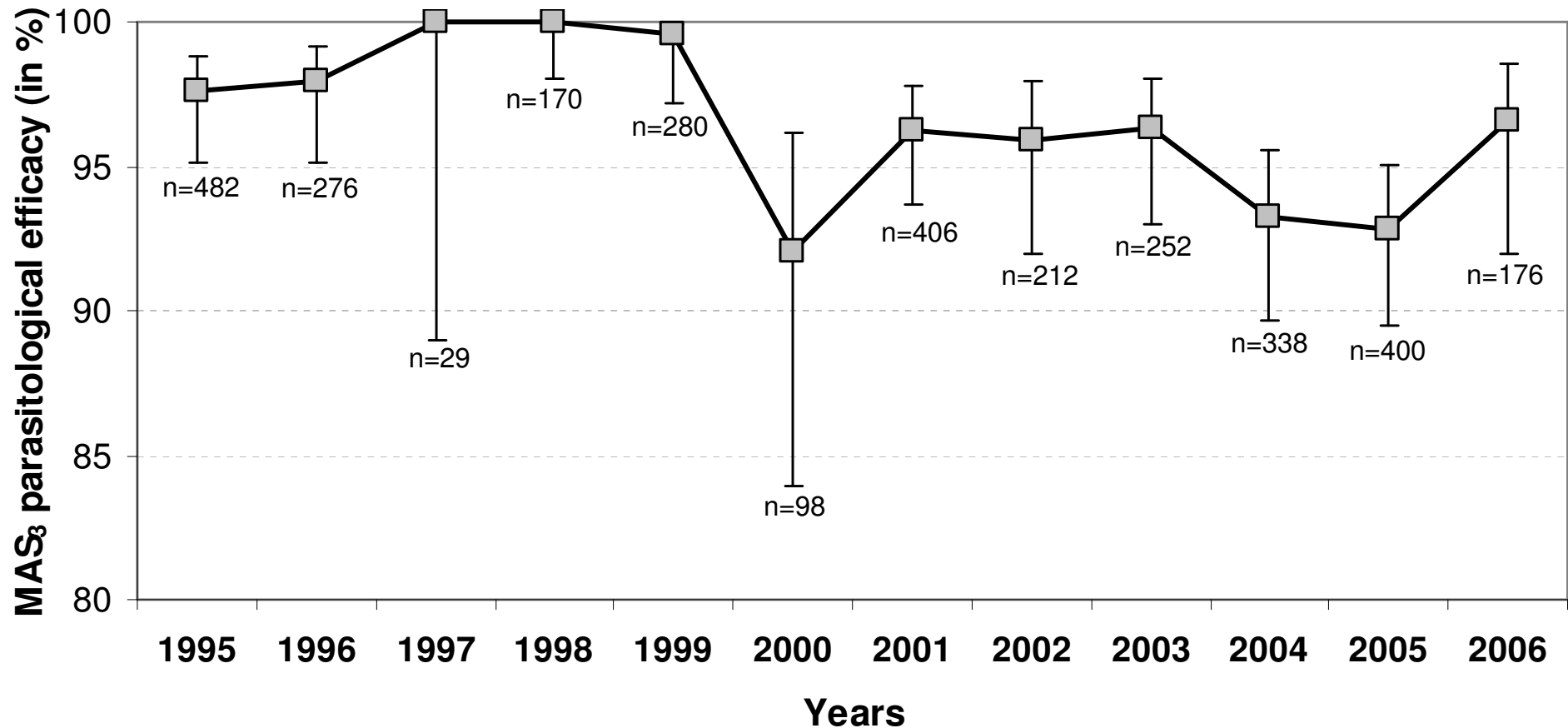
Parasite clearance

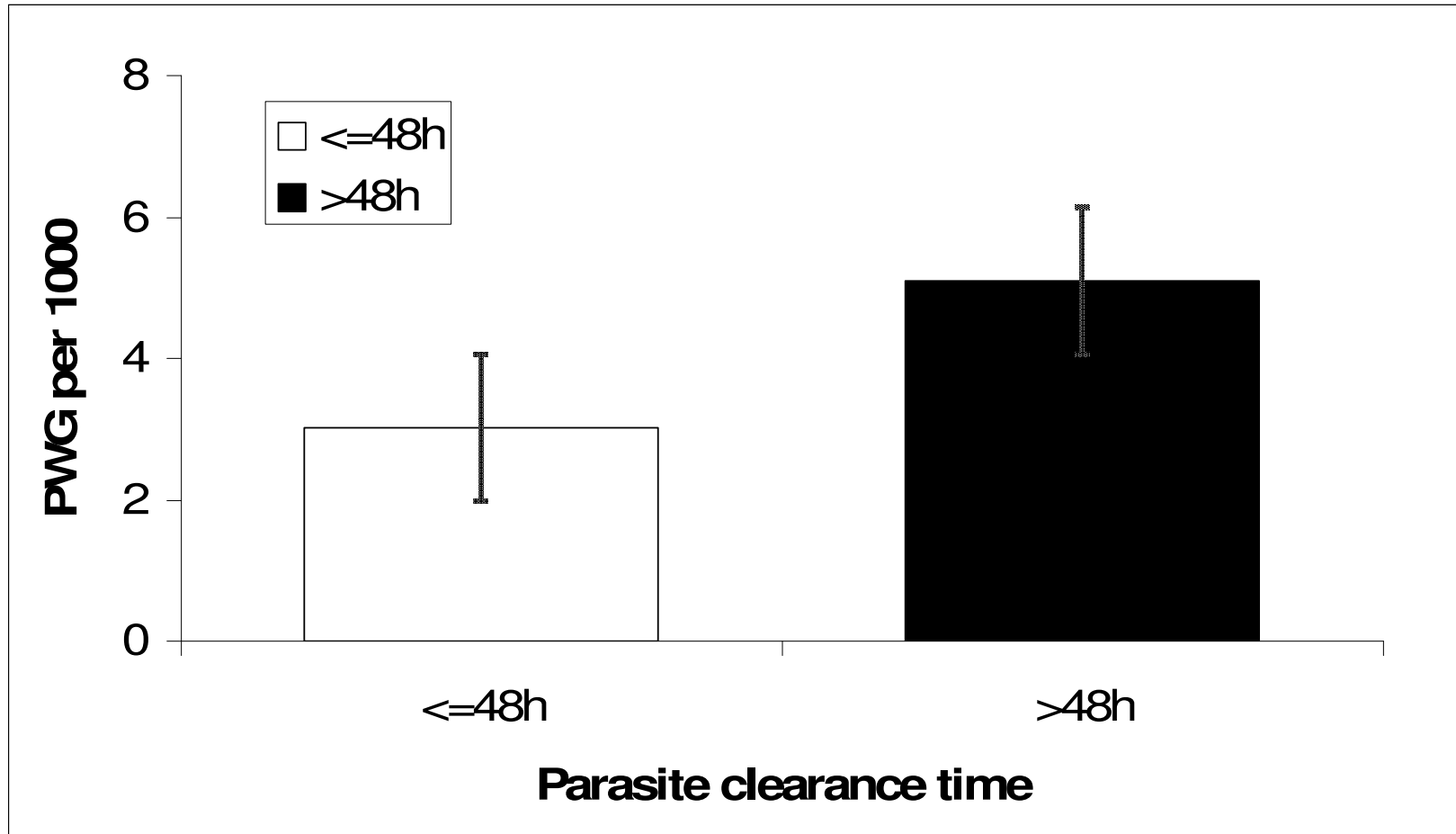


Recurrent *P. falciparum* infections

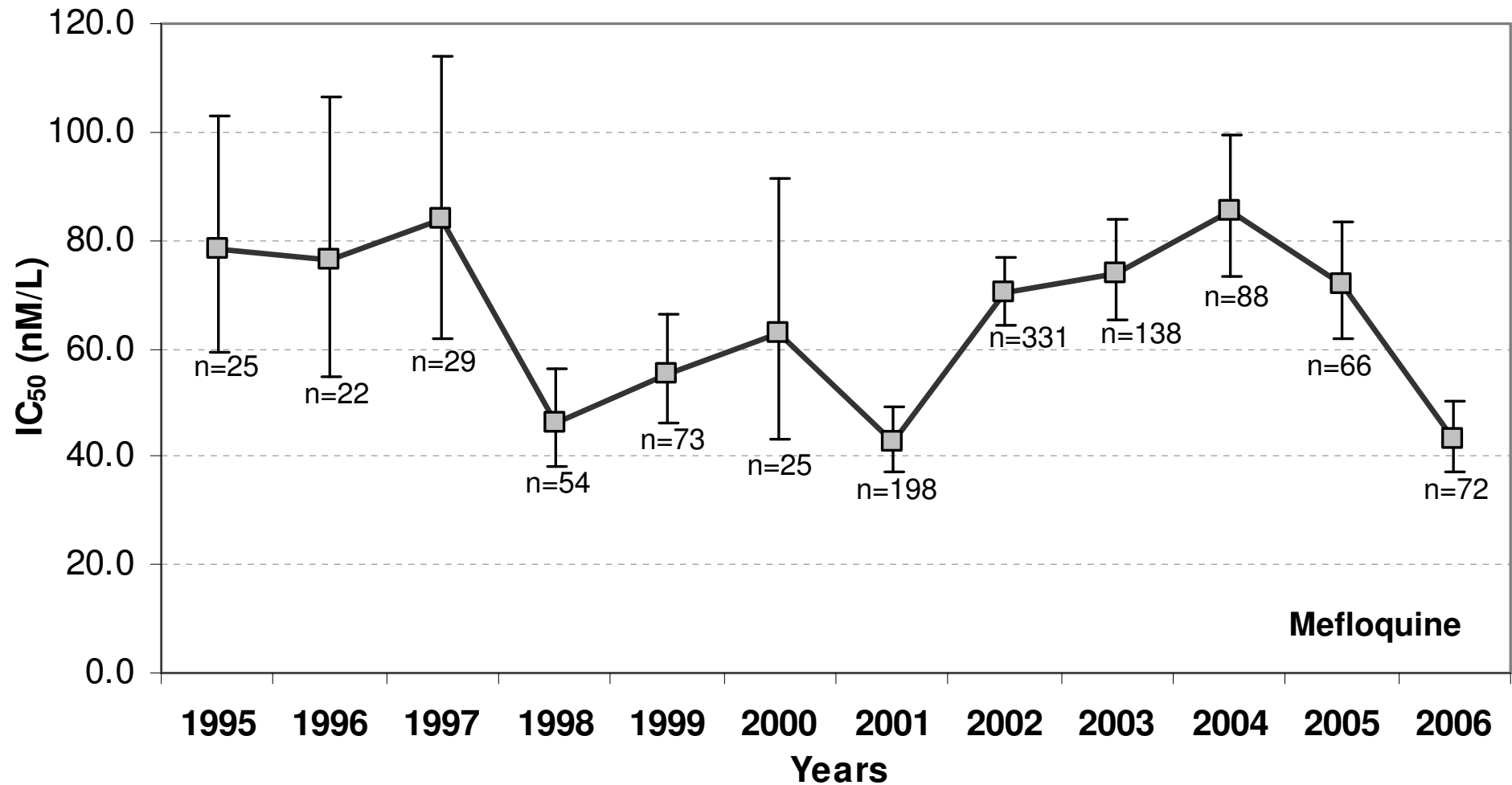
Total recurrent infections with <i>P. falciparum</i>	315
Novel infections (N)	167 (53%)
Recrudescence Infections (N)	102 (32%)
PCR Not Done (N)	22 (7%)
Indeterminate (N)	15 (5%)
Missing (N)	9 (3%)
Days to recrudescence (median, range)	21 [7-42]

PCR-adjusted parasitological efficacy at Day 42



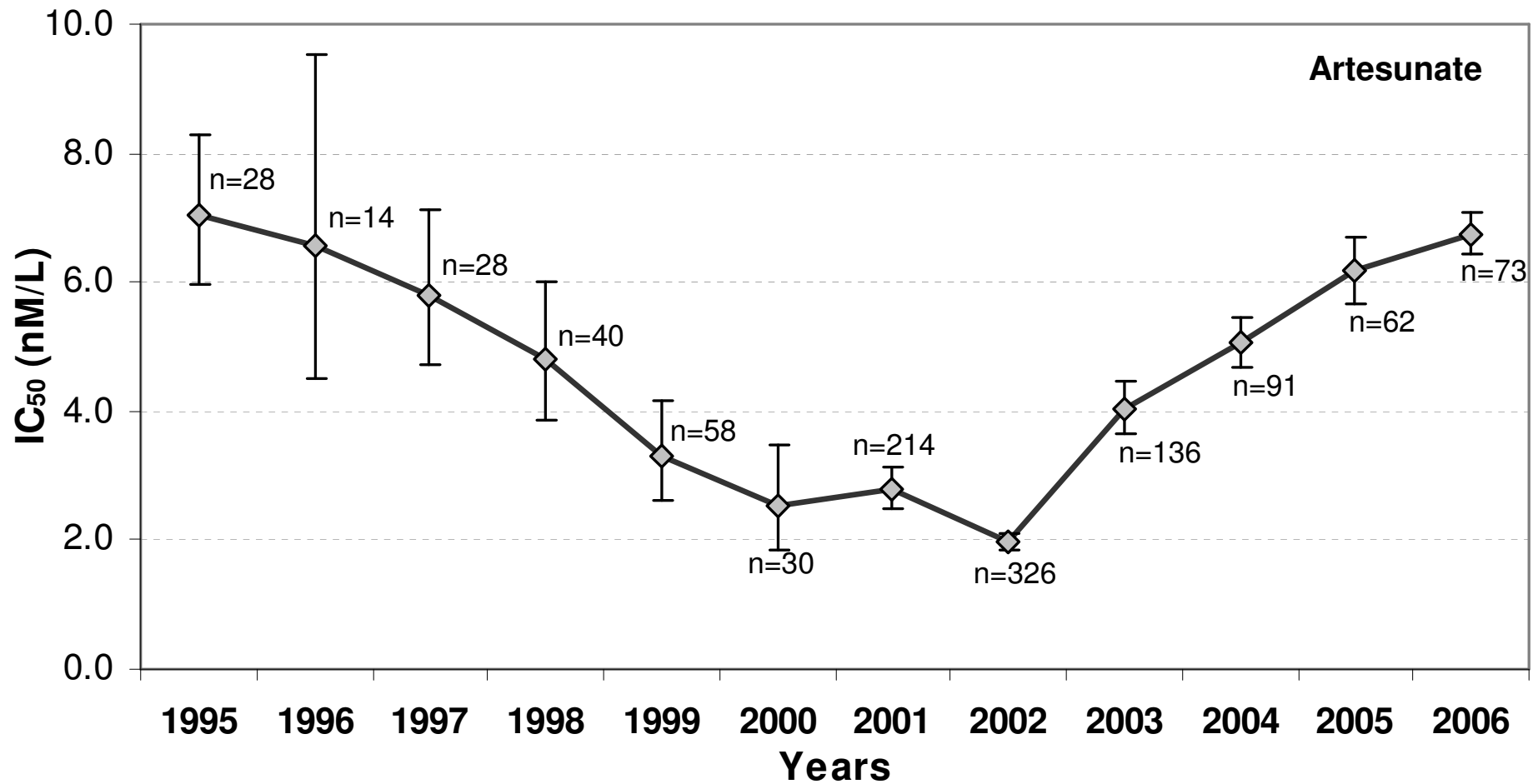


In-vitro susceptibility to mefloquine



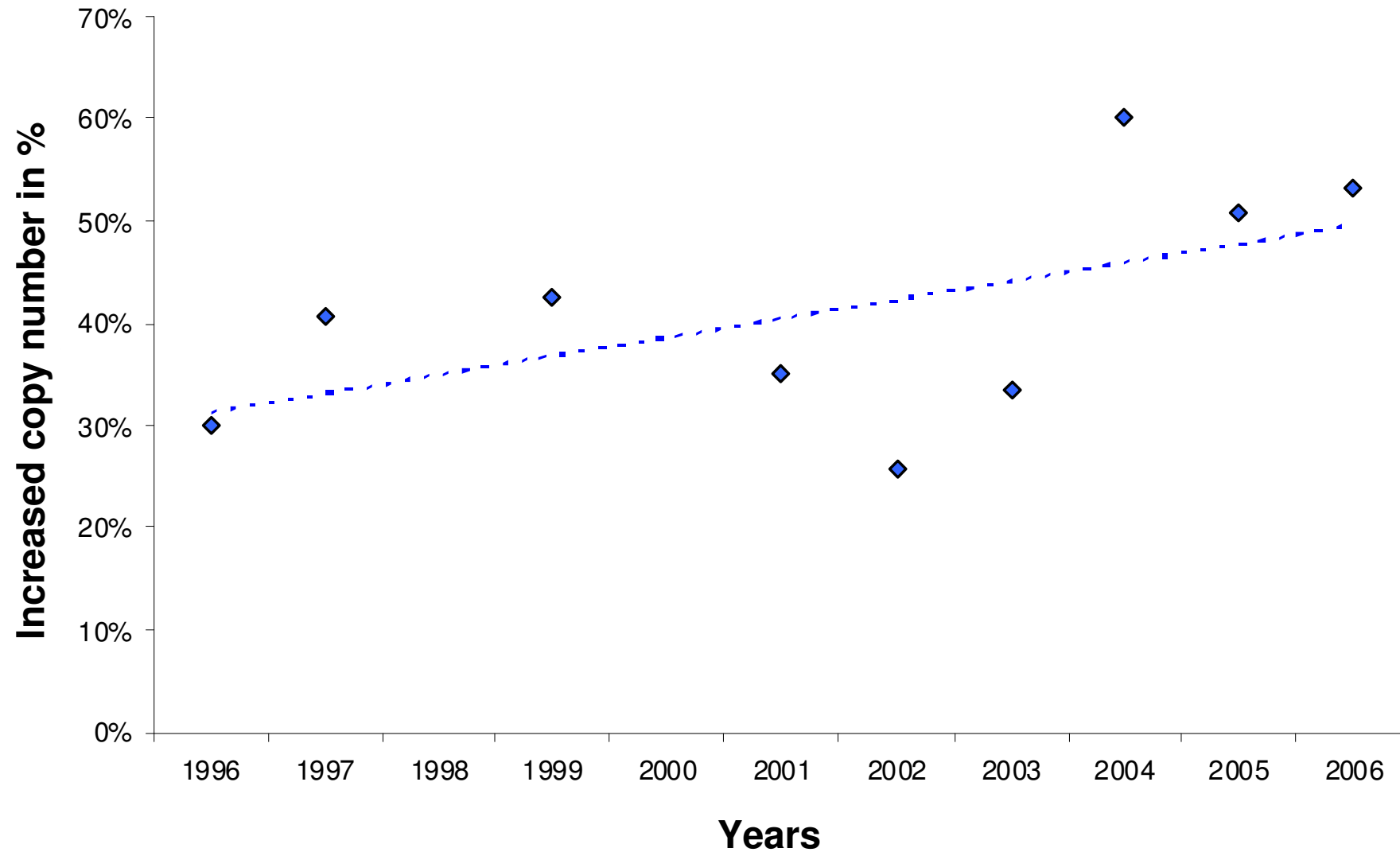
(Values in geometric mean IC_{50} with 95% CI)

In-vitro susceptibility to artesunate



(Values in geometric mean IC₅₀ with 95% CI)

Pfmdr1 (≥ 2) copy number trend



In summary

- *No significant change in mefloquine and artesunate susceptibility in-vitro*
- Prolongation of parasite clearance times
- 2007(till Nov. result) 15 out of 67 (22%) of patients still have parasitaemia on Day 2 of treatment
- Higher proportion of isolates with increased *pfmdr1* copy numbers

A small but significant decline in MAS₃ parasitological efficacy

Conclusion

- Recent findings in Cambodia show ~50% of the patients treated with artesunate still have parasitaemia on Day 3 of treatment
- A very close monitoring of the susceptibility of *P.falciparum* in this area to detect the possible emergence of artemisinin resistance
- The systematic recording of parasite clearance times during clinical trials is strongly recommended.

Thanks to:



- Patients
- Medical teams
- Bangkok Wellcome-Unit Laboratory &
- Statistics departments

