Research priorities in vector biology for better malaria control in Southeast Asia

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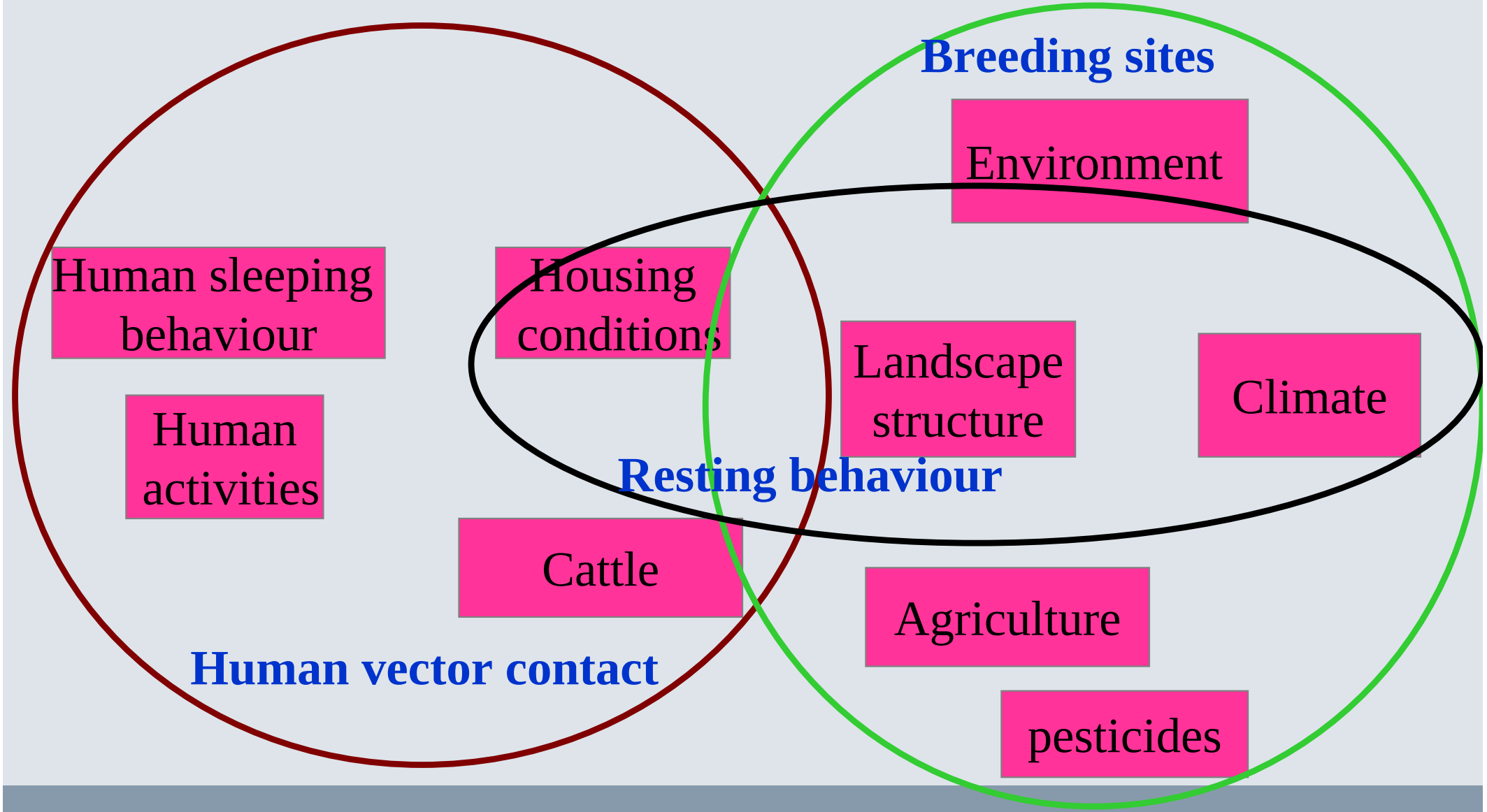
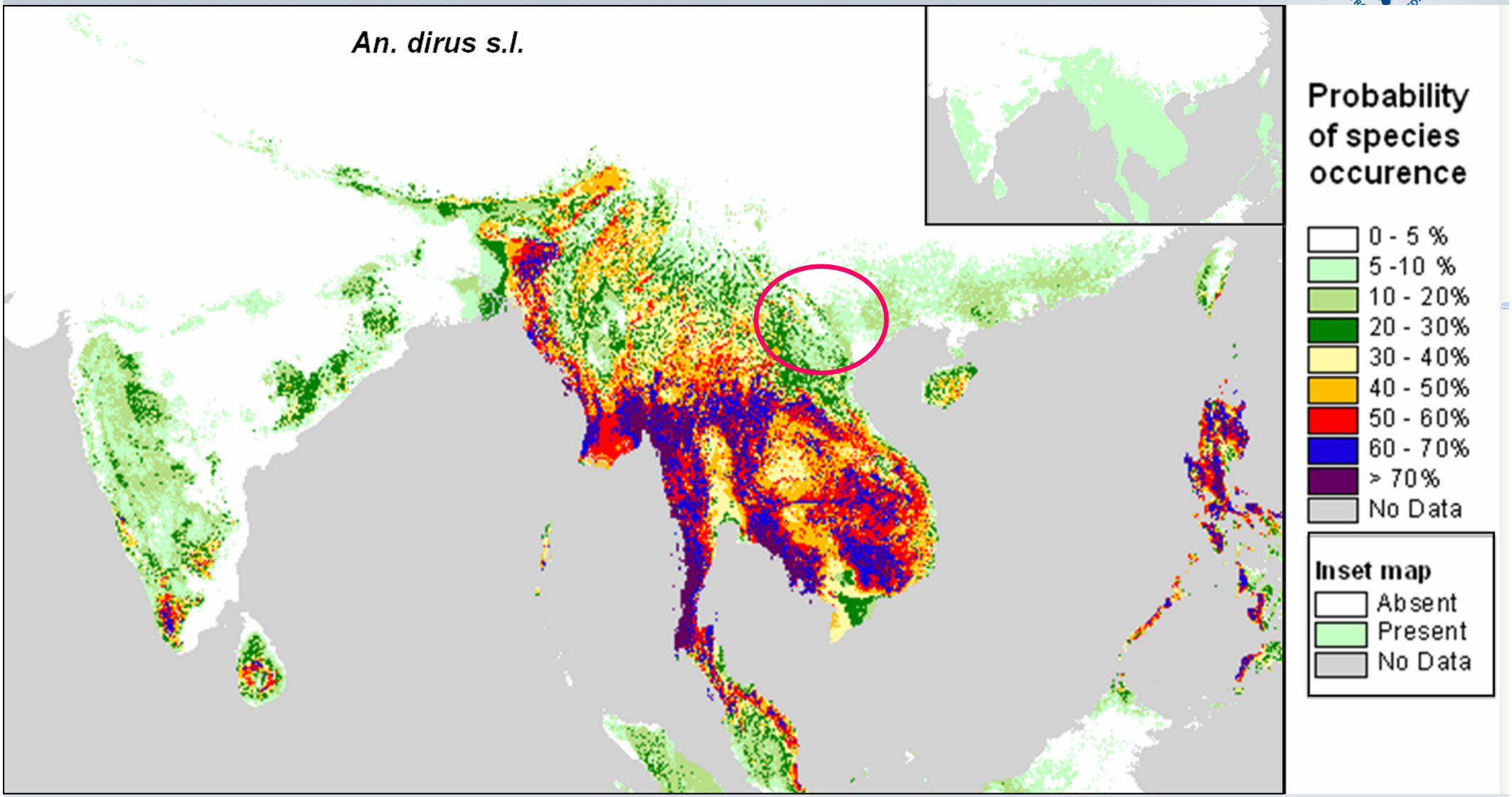
Malaria vectors: parameters

Genetical background



Fundamental niche of *An.dirus* s.l.
(Obsomer et al. 2010)

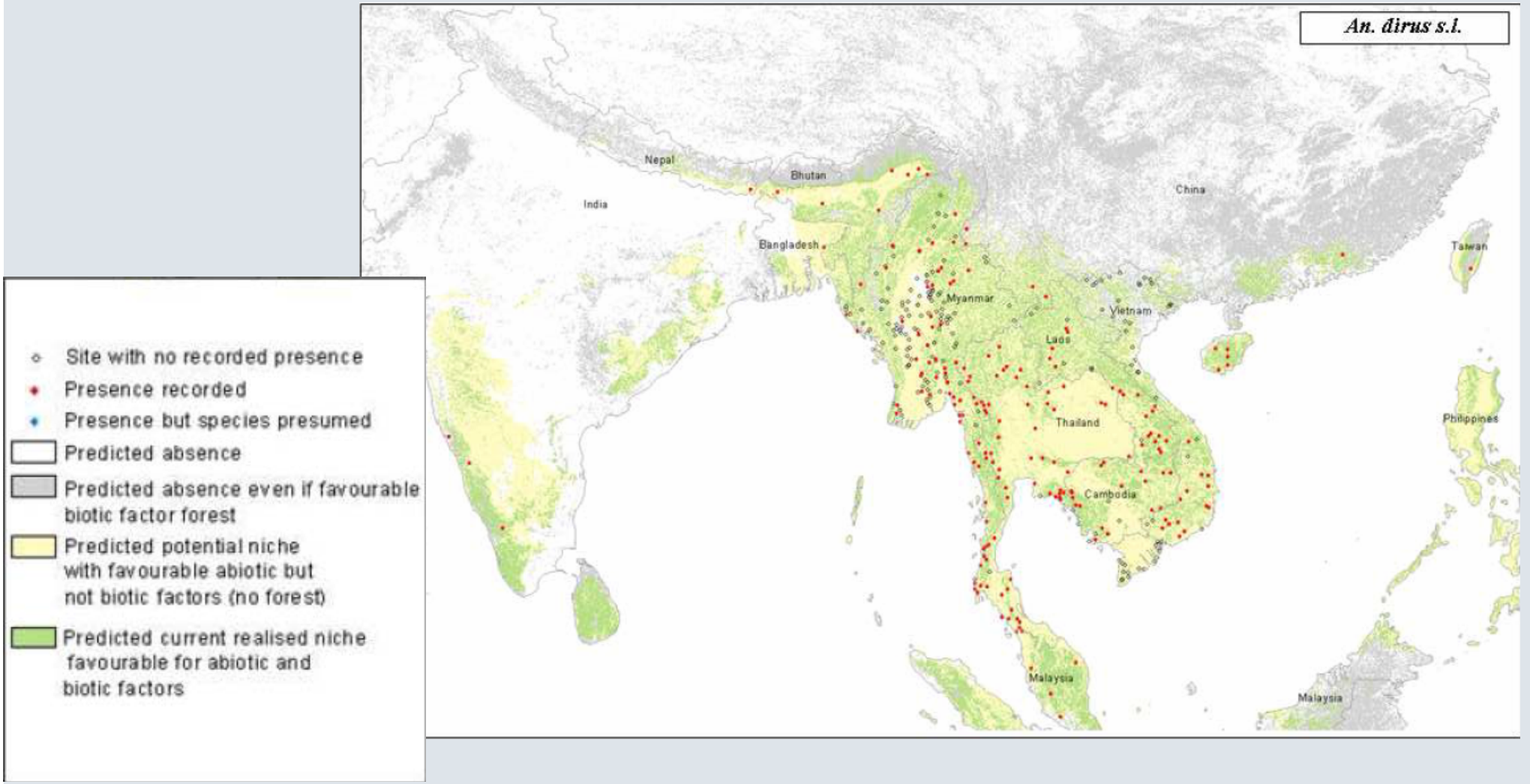


Suitability map from 0 to 100% based on long term climate trends and topography

Converted to a Presence/absence map using a optimized threshold value

Realized niche of *An.dirus* s.l.

(Obsomer et al. 2010)



OPERATIONAL RESEARCH:
Changing ecology and behaviours of vectors

The principal vector: *An.dirus* sensu lato

- the most effective vector in the region even at (very) low densities.
- Distribution is associated with forest but deforestation reducing suitable habitats.

⇒ **Capacity of adaption to fragmented forest and to human-made habitats such as orchards and plantations?**

- Ecological niche and environmental influences of *An. dirus s.l.* have been defined at the continental/ regional scale but not at the local level.

⇒ **their seasonal variation in distribution and movements (including maximal seeking behaviour) is essential for assessing the malaria risks and targeting these vector populations**

⇒ **where do they stay during the dry season? Deep forest? Evergreen "islands "**

OPERATIONAL RESEARCH: changing ecology and behaviours of vectors

Secondary vectors:

- Vector status of an anopheles species might vary according to modifications of the environment:

⇒ **Role of secondary vectors and potential vector species**

⇒ **Prediction models of species and transmission occurrence at local level is needed.**

- Species identification on morphological characters is not (fully) reliable.

=> Need for additional molecular tools

Sampling: HLC

Human landing collections:

- The most direct method for addressing only man biting mosquitoes
- Asses the degree of exophagy and vector biting times

ISSUES

- labor intensive: limited data points (space and time)
- vigilance throughout the night + intense supervision
- variability in attractiveness + skills collectors
- likely to catch more than under natural conditions (particularly when ITNs are used)
- Interrupted multiple feeding during one night: underestimated by HLC.
- ethical concerns

Sampling: traps

CDC light trap:

- Less labour intensive
- Many data points possible
- Effective range: less than 5m,
- Presence in a hut is unlikely to attract more mosquitos into it.
- Ethically acceptable

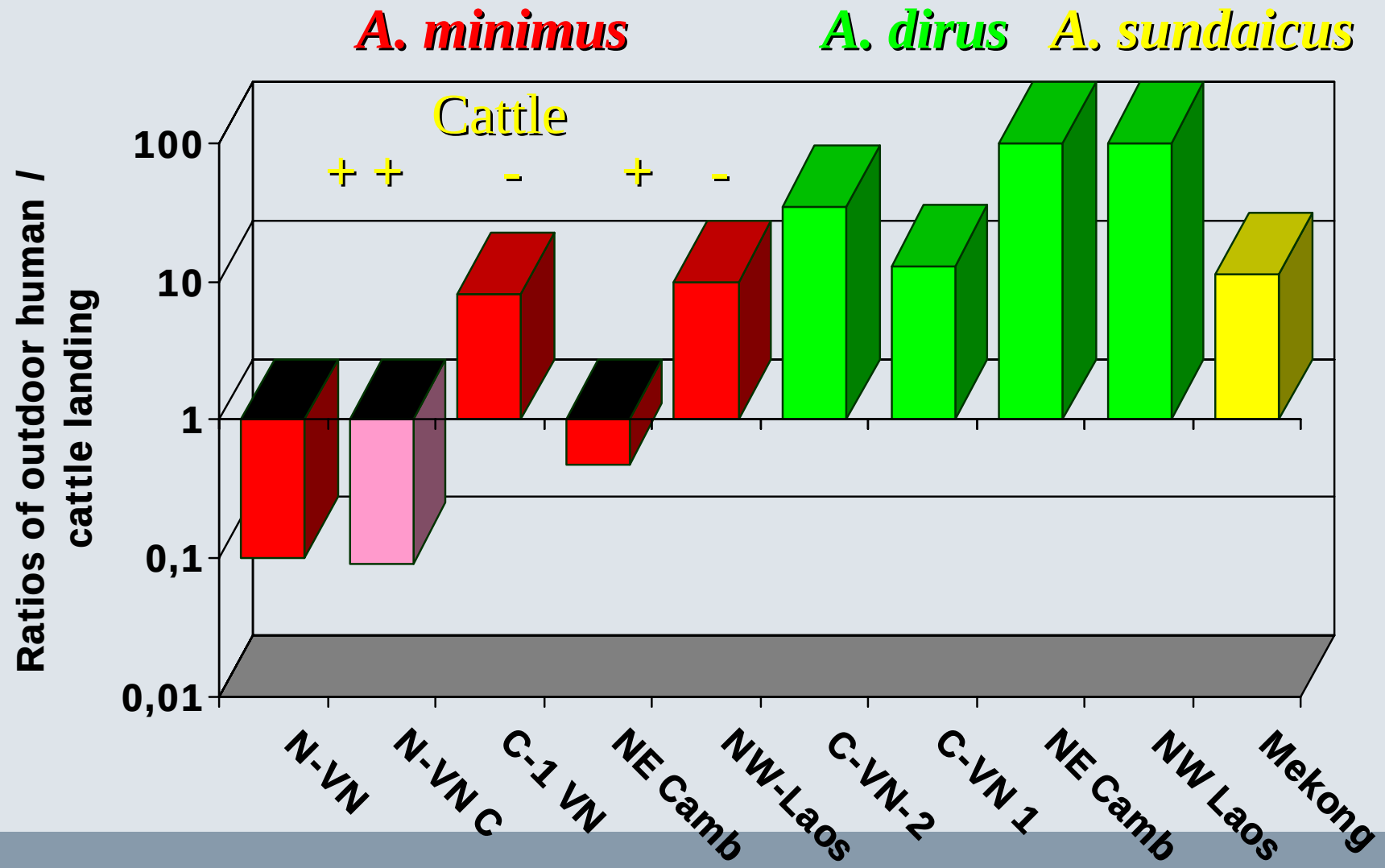
ISSUES

- Not reliable outdoors. Only effective for collecting indoor host-seeking mosquitoes
- Vector biting times not possible
- Validation in relation to HBC locally
  - Vector species composition
  - Intraspecific variation in feeding and resting behaviour
  - Attract a portion of non-host-seeking vectors (other species, resting specimens)
  - Trap efficiency not always density independent
  - Sporozoite rate sometimes different (2 fold higher - Davis et al 1995, Mbogo et al 1993)
  - Trap placement: close to host acting as bait/ host under net

Man biting rate: Traps

Will LT reflect the human biting population?

Adapted from Trung et al. 2005



Man biting rate: Human landing collections

Biting activity before 22.00h (OUTdoors)

Cumulative biting rate of Anopheles species in Ninh Thuan prov (Vietnam)

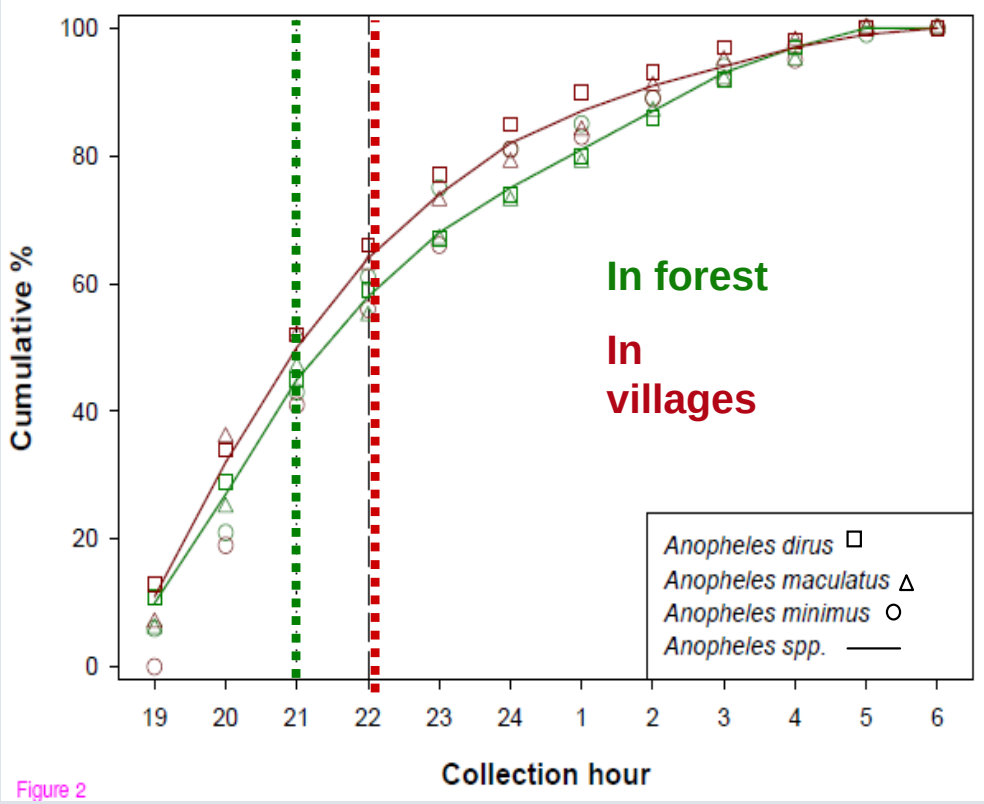


Figure 2

% of bites before 22h in the villages

	maculatus	*minimus*	*dirus*
Pailin (C)	52.6%	23.3%	22.4%
Pursat (C)	63.2%	48.3%	35.2%
Ninh T (V)	64.4%	62.3%	62.1%

Van Bortel et al. 2010 MJ submitted;

Sochantha et al. 2010

TRANSMISSION: Cumulative infective bites in the forest

Ninh Thuan province (Vietnam) Van Bortel et al. 2010 MJ submitted

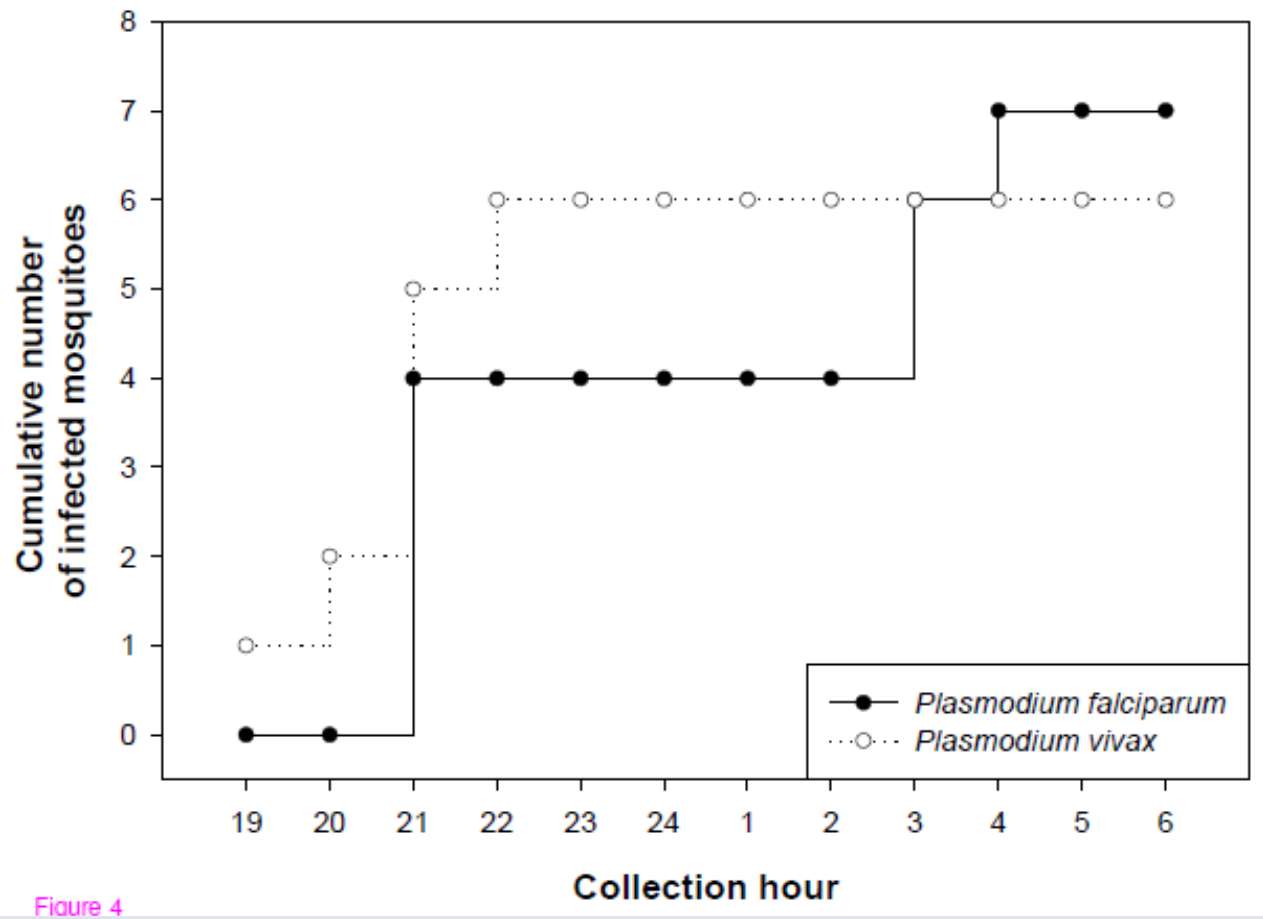
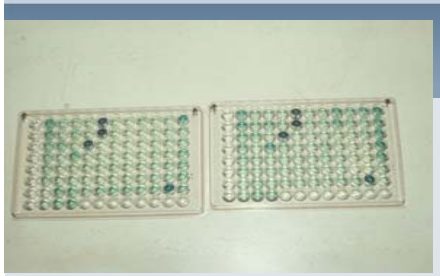


Figure 4

=> Transmission occurs in the evening and early morning species

The sporozoite index

Confirmation Pf-CSP ELISA

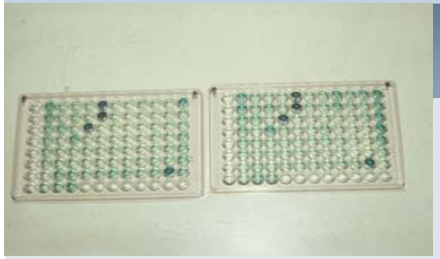


	Cambodia			Vietnam		
	N° Tested	N° ELISA +	N° PCR confirmed	N° Tested	N° ELISA +	N° PCR confirmed
Anthropophilic	**1138**	**12**	**10**	**883**	**13**	**8**
An. dirus	1138	12	10	883	13	8
Zoophilic	**7996**	**113**	**1**	**6209**	**48**	**1**
An. barbirostris	1632	38	0			
An. jamesii	16	1	0			
An. maculatus	3518	53	1	5220	42	0
An. minimus	2830	21	0	547	4	1
An. pampanai				77	1	0
An. splendidus				365	1	0

=> Many false Pf ELISA positives in zoophilic species (Durnez et al 2010 in prep)

The sporozoite index

Confirmation Pv-CSP ELISA



	Cambodia			Vietnam		
	N° Tested	N° ELISA +	N° PCR confirmed	N° Tested	N° ELISA +	N° PCR confirmed
Anthropophilic	**1138**	**5**	**3 (+ 1)***	**883**	**3**	**3**
An. dirus	1138	5	3 (+ 1)*	883	3	3
Zoophilic	**7994**	**3**	**2 (+ 1)***	**6209**	**6**	**3**
An. barbirostris	1632	1	0 (+ 1)*			
An. jamesii	16	0	0			
An. maculatus	3518	1	1	5220	5	2
An. minimus	2828	1	1	547	0	0
An. pampanai				77	1	1
An. splendidus				365	0	0

+ 1: *P. malariae* instead of *P. vivax*

=> FEW false Pv ELISA positives, but not specific

(Durnez et al 2010 in prep)

TRANSMISSION: where does it occurs?

Table 2. Overview of the *Plasmodium* infected mosquitoes as detected by ELISA and confirmed by PCR.

Van Bortel et al. 2010 MJ submitted;

Collection place	*Anopheles* species (morphological identification)	Number of *Plasmodium* sporoziote infected mosquitoes (number tested)		
		P. falciparum	*P. vivax 210*	*P. vivax 247*
Forest	*An. dirus*[1]	6 (642)	2 (642)	2 (485)
	An. maculatus s.l.[2]	0 (3454)	0 (3454)	2 (1826)
	An. minimus s.l.[3]	1 (264)	0 (264)	0 (166)
	An. pampanai[4]	0 (23)	0 (23)	1 (23)
Way	*An. dirus*[1]	2 (151)	0 (151)	0 (103)
	An. maculatus s.l.	0 (618)	0 (618)	0 (524)
	An. minimus s.l.	0 (204)	0 (204)	0 (144)
	An. pampanai	0 (37)	0 (37)	0 (37)
Village	*An. dirus s.l.*	0 (71)	0 (71)	0 (43)
	An. maculatus s.l.	0 (1009)	0 (1009)	0 (650)
	An. minimus s.l.	0 (62)	0 (62)	0 (41)
	An. pampanai	0 (5)	0 (5)	0 (5)

[1]All ELISA positive specimens were molecular identified as *An.dirus s.s.*
[2]All ELISA positive specimens were molecular identified as *An.sawadwongporni*
[3]The ELISA positive specimen was molecular identified as *An.minimus s.s.*
[4]The identification of the ELISA positive specimen was molecular confirmed as *An.pampanai*

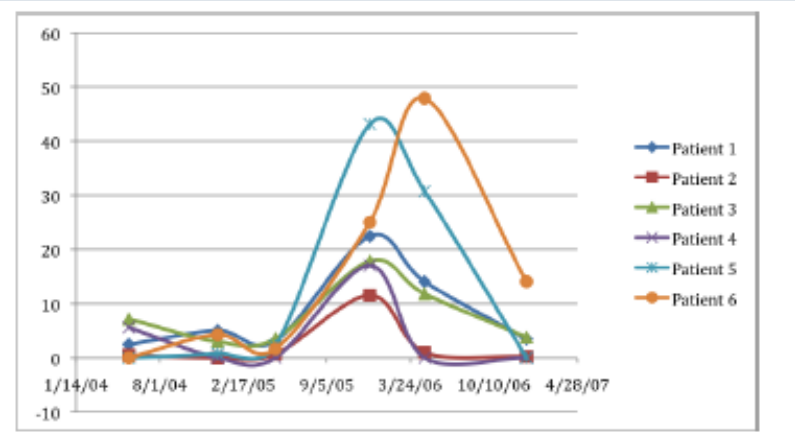
=> Transmission occurs mainly in forest plots

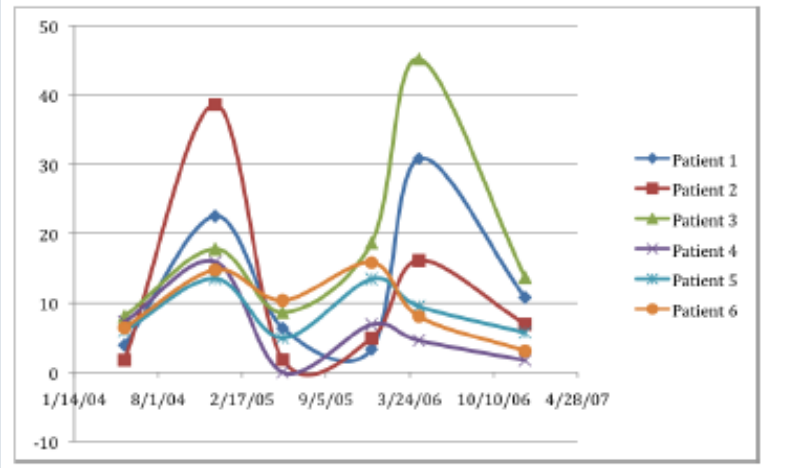
OPERATIONAL RESEARCH
Mosquito collecting methods and EIR

- ⇒ Need for **standardization**: data points (time-space), mosquito collecting methods, species determination, PCR confirmation of ELISA+ mosquitoes
- ⇒ The human landing catch should be maintained as the **standard reference** method for use in calibrating new methods for sampling the human biting population of mosquitoes and this in each locality.
- ⇒ Need for estimation of **OUTDOOR** EIR (mainly before sleeping time)
- ⇒ Addressing the issue of **heterogeneous biting** : 20% of people receive 80% of all infections. (Woolhouse et al 1997)

OPERATIONAL RESEARCH
Assessing the force of infection

where transmission is very low





Serological surveillance:

possibility of estimating incidence of infection by using changes in antibody titres.

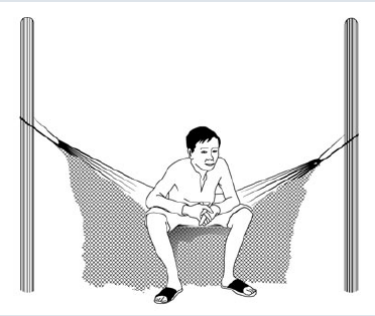
Claes et al. 2010 submitted)

Vector Control

- IRS: endophily very low
- LLINs:
  - nets not distributed to mobile populations (including adolescents)
  - Low adherence to polyethylene nets
  - Forest workers? (In VN Ra-glai community: 85% use nets in the villages but only 53% in the forest plots Peeters et al 2010)
  - Population not protected in the evening and early in the morning!

=> Need for additional personnel protection!!

Protective effect of Long lasting insecticidal hammocks (Sochantha et al. 2010; Thang et al. 2009)



Species	Period	Interaction treatment w	% reduction
Culicines	• Whole night • Before 22h	Village Village	**28.7** (9.1-44) **36.5** (21.5-48.7)
A.maculatus	• Whole night • Before 22h	Village Village	**49.8** (30.9-63.5) **55.9** (35.9-69.7)
A.dirus	• Whole night • Before 22h	Survey Vil/Survey	**46.3** (25.3-61.5)
A.minimus	• Whole night • Before 22h	No no	**45.5** (34.7-54.5) **44.5** (25.0-58.9)

Randomized control trial in VN:

- malaria infection: 1.6 fold reduction
- incidence: 2 fold reduction

OPERATIONAL RESEARCH:
Innovative strategies for personal protection

- **Proof of principle**
  - (Spatio-)Repellents: (different a.i? and formulations)
  - Insecticide treated hammocks, clothing
  - Treated Plastic sheeting
  - Mosquito Coils/ vaporizers
  - *Krahmas* (multi-functional traditional scarves) impregnated with insecticide? BUT used for multi-purposes and often washed; close contact with skin!
- **Efficacy studies (Randomised community based trials??)**
- **Acceptability & feasibility studies**

OPERATIONAL RESEARCH:
Innovative strategies for personal protection

Adapting LLINs to the needs for forest workers

Netprotect A

- especially adapted to non-permanent sleeping places;
- easy to suspend in two points, easy to push away in day time.
- Lower part with double layer.

OPERATIONAL RESEARCH: Monitoring Insecticide resistance

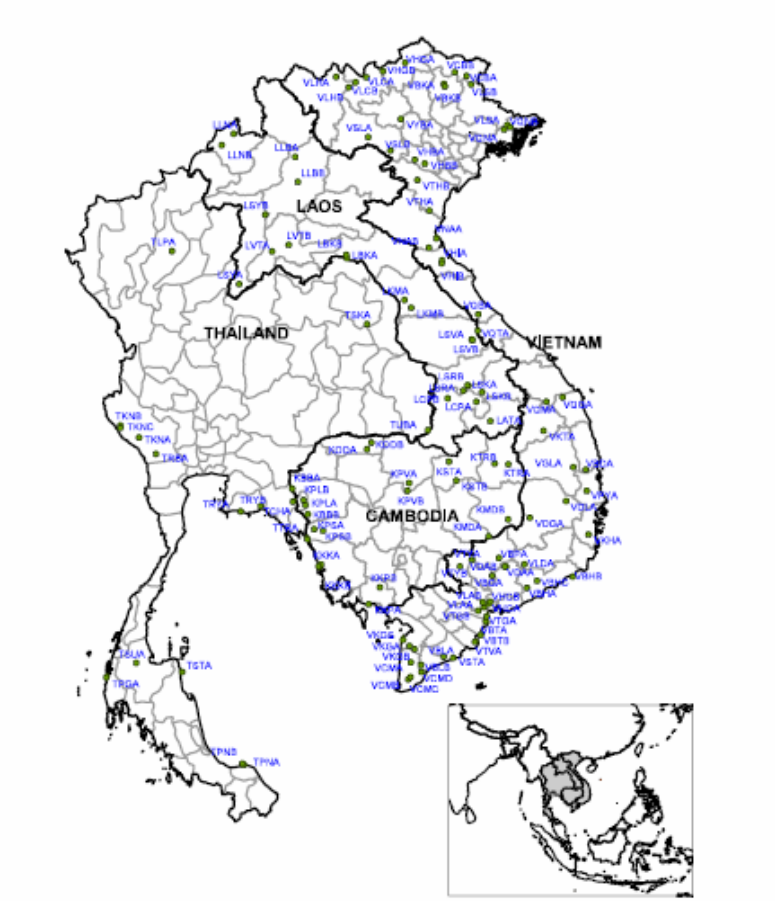


Figure 1
The MALVECASIA study sites with their corresponding codes.

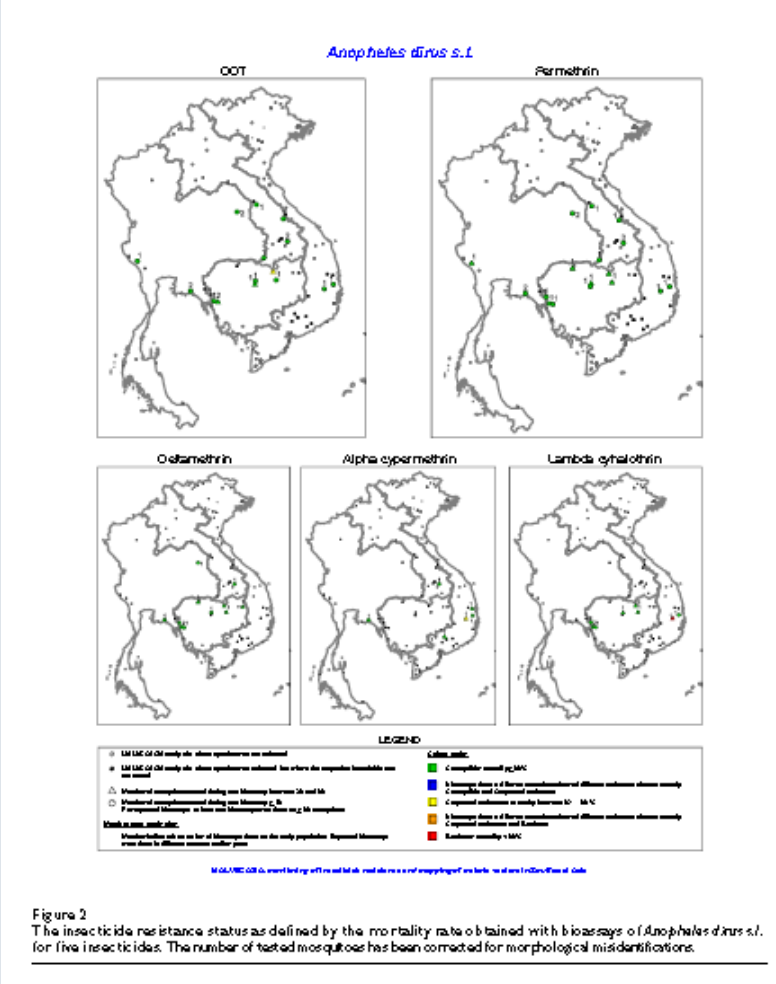


Figure 2
The insecticide resistance status as defined by the mortality rate obtained with bioassays of *Anopheles dirus* s.l. for five insecticides. The number of tested mosquitoes has been corrected for morphological misidentifications.

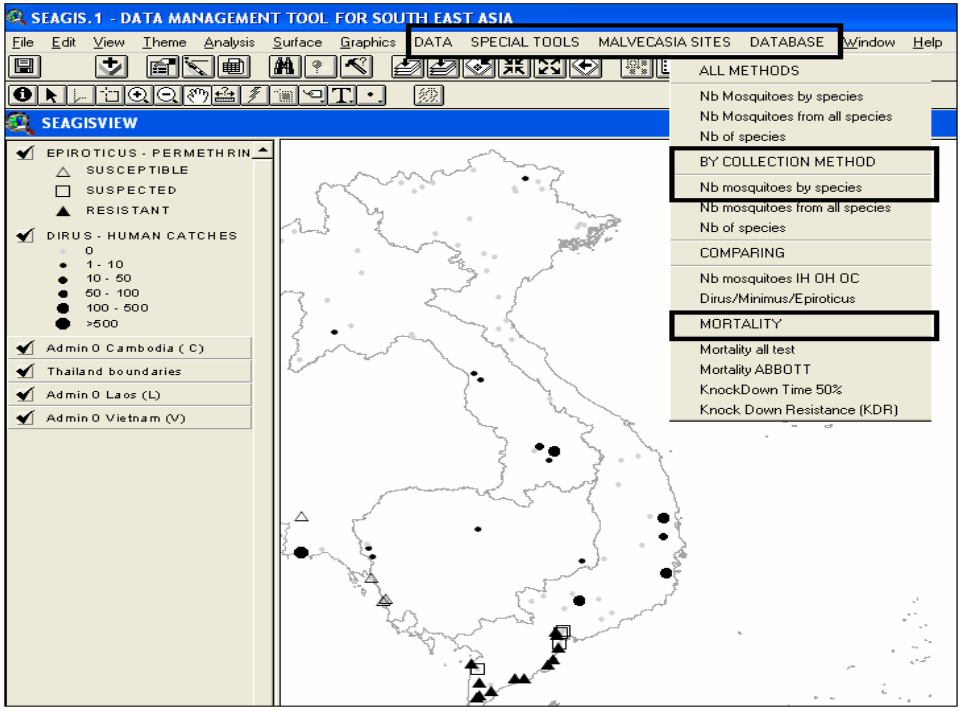
Van Bortel et al 2008

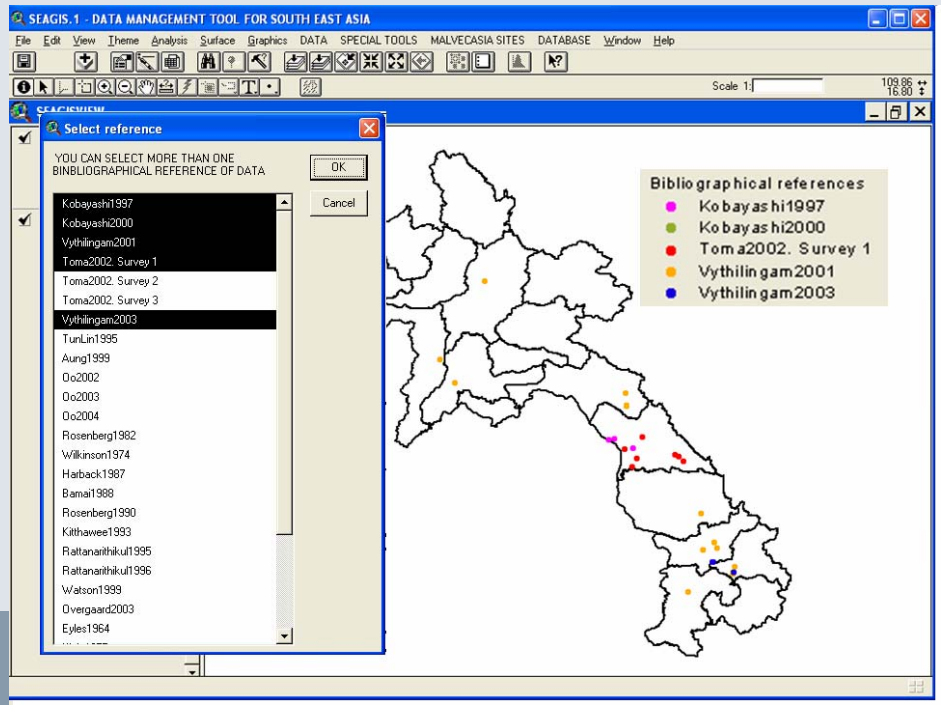
=> Need for updating + database

OPERATIONAL RESEARCH
Regional data base and mapping

- Development of Geographic Information Systems to integrate data from various sources, formats and themes (vector distribution, insecticide resistance, updated land cover, climate changes, etc) can provide a user friendly interface to make information available for control programme managers.

=> One system exist –SEAGIS- but should be updated





CONCLUSIONS

- Large distribution of LLINs is essential but not enough as about 30 to 50% of the transmission occurs before sleeping time (vectors are early biters) or in the early morning, moreover forest workers and mobile people (which are the most at risk) have little compliance with using nets.

- Better understanding of vector behaviour and distribution is needed taking into account the high variability from site to site.

- New tools to protect forest workers and mobile population are urgently needed.

Kop khun khrap

Merci beaucoup

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