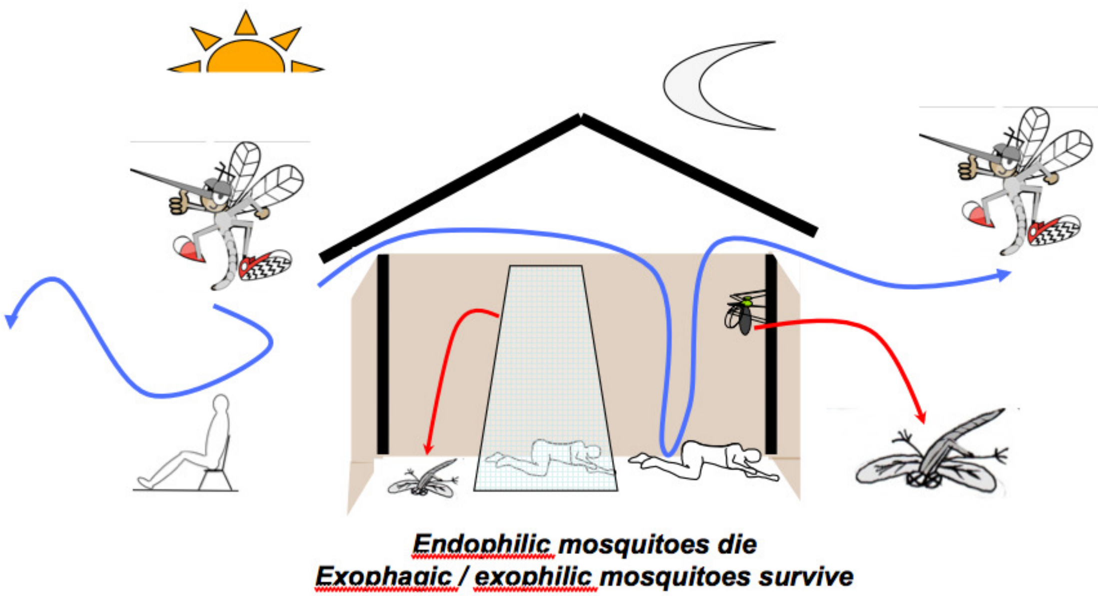
Topical and spatial repellents: where are we?

5th Outdoor Malaria Transmission
Work Stream Meeting
Wednesday 30th January 2013 13:00-15:00

Sarah J Moore, LSHTM and Ifakara Health Institute

Benefits of outdoor and early evening feeding when people have intra-domicillary control tools



Host availability

Inter-specific larval competition

ROLL BACK MALARIA

SOUTH AMERICA

Country	Vector	% biting outside of sleeping hour	% biting outdoors	Sampling method	Ref
Belize	*An. albimanus*	20.83	79.47	HLC	(52)
	An. darlingi	15.25	82.57		
Belize	*An. darlingi*	-	49.08	HLC	(53)
	An. albimanus	-	24.47		
Bolivia	*An. darlingi*	83.0	-	HLC	(54)
Brazil	*An. darlingi*	57.21	73.74	HLC	(55)
	An. darlingi	-	75.77	HLC	(56)
Dominican republic	*An. albimanus*	85.3	77.3	HLC	(59)
French Guiana	*An. darlingi*	-	68.88	HLC	(57)
Suriname	*An. darlingi*	13	62.86	HLC	(58)

Average 45.8% biting before bed-time

Average 66% outdoor feeding

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MEKONG REGION

Vector		Country	% biting before 21.00h	indoor: outdoor biting	Ref
An. dirus complex (Peyton and Harrison, 1979)	Subspecies not identified	Myanmar	7.1%	-	[1]
		Thailand	20.7%	-	[2, 11]
		Lao PDR	-	1.1	[4]
		Lao PDR	-	0.67	[12]
		Cambodia	-	2.00	[13]
		Lao PDR	19.0	-	[7]
		Thailand	6.3%	-	[15]
	An. dirus (species A)	SE Asia	-	0.32-1.3	[3, 16]
		Thailand	23.8%	-	[15]
	An. cracens (Species B)	Thailand	50.8%	-	[15]
	An. scanloni (Species C)	Thailand	76.1%	-	[15]
An. maculatus (Theobald, 1901)		Malaysia	-	0.37	[6]
		Philippines	-	All outdoors	[8]
		Cambodia	-	0.29	[13]
		Lao PDR	53.3%	-	[7]
		Philippines	30.6%	0.39	[23]
		SE Asia	-	0.08-0.19	[3]
		Lao PDR	-	0.26	[4]
		Myanmar	38.8%	-	[1]
		Thailand	64.1%	-	[2, 11]
		Malaysia	-	88.9%	[25]
An. minimus group	Subspecies not identified	Lao PDR	-	0.54	[4]
		Lao PDR	-	0.50	[12]
		Cambodia	-	1.21	[13]
		Myanmar	26.2%	-	[1]
		Lao PDR	23.5-45.8	-	[7]
		Thailand	15.7%	-	[2, 11]
		Thailand	Peak 18.00-21.00	Higher outdoor	[28]
		Vietnam	-	0.82	[29]
	An. minimus A	SE Asia	-	0.62-7.95	[3, 16]
		Thailand	-	0.19	[30]
	An. minimus C	SE Asia	-	0.35	[3]
		Thailand	-	0.19	[31]
An. sinensis		Myanmar	69.8%	-	[1]
		SE Asia	-	0.17-0.88	[3]
		Malaysia	-	0.36	[6]
An. stephensi (Liston, 1901)		Myanmar	50.0%	-	[1]
An. sundaicus (Rodenwaldt, 1925)		SE Asia	-	1.27	[3, 16]
		Myanmar	49.1%	-	[1]

Average 38.5% biting before bed-time

Average indoor : outdoor ratio 0.9 and 0.6 if you exclude *An. minimus* A

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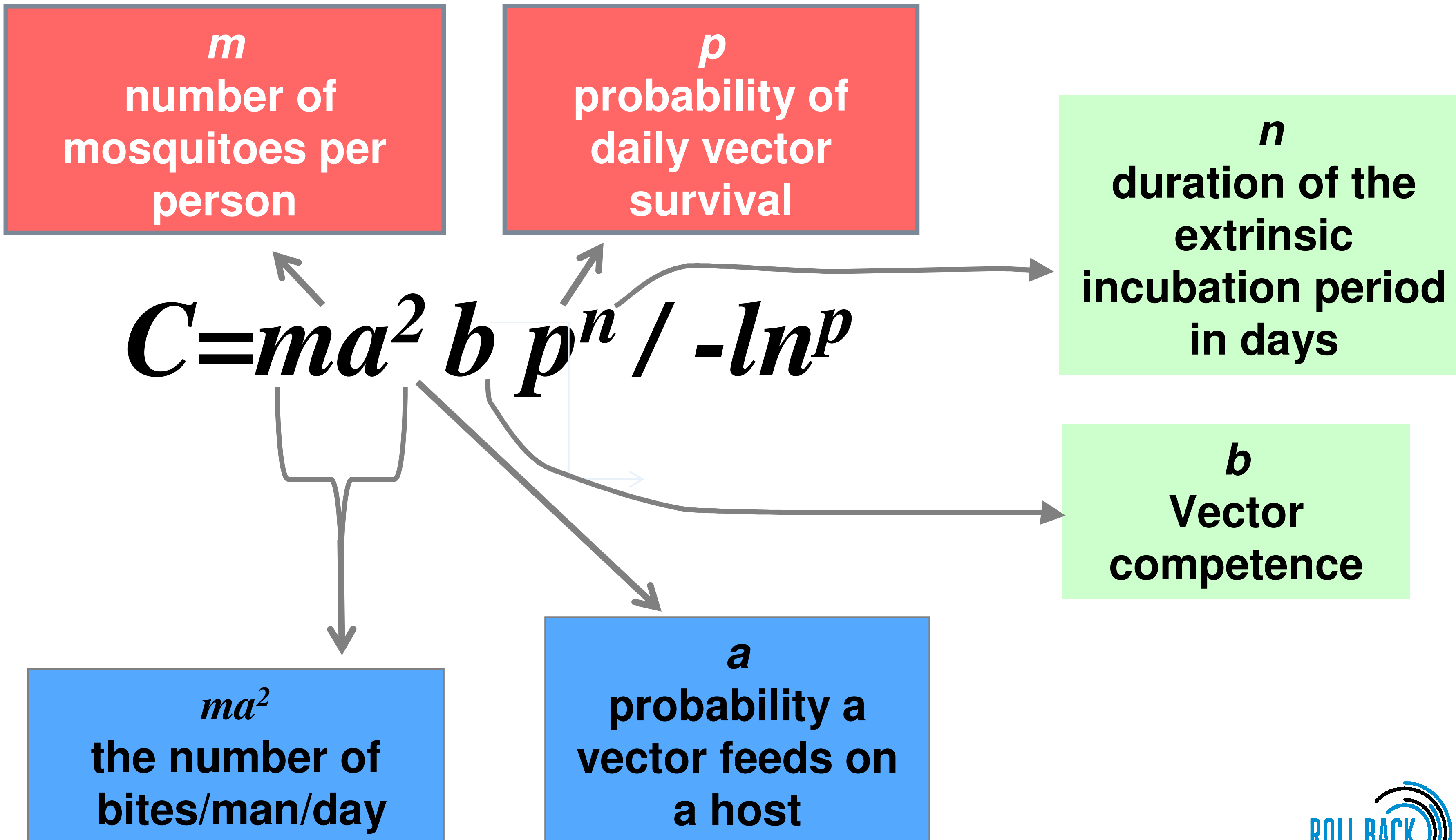
Occupational exposure

Transient *non-immunes*

Vectorial capacity: a means of conceptualising the impact and mode of action of an intervention



Disease		Intervention		Design
malaria		repellent		Trial
OR		OR		OR
dengue		DEET		Community
OR		OR		OR
leishmaniasis		clothing		“Case control”
		OR		OR
	AND	coil	AND	Questionnaire
		OR		OR
		metofluthrin		“Cross sectional”
		OR		OR
		transfluthrin		“Cohort study”
				OR
				military

- **RCTs >Cohort and case control trials >cross-sectional and observational studies with local populations > cross-sectional and observational of travellers.**

- **Outcomes - parasite rates of disease measured by standard methodology e.g. blood smears or rapid diagnostic tests for malaria.**

- **Risk of bias and confounding: design, recruitment methodology, generation of treatment allocation, randomization of treatments, allocation concealment, blinding, implementation of study and reporting of results**

- **New infections in person years**

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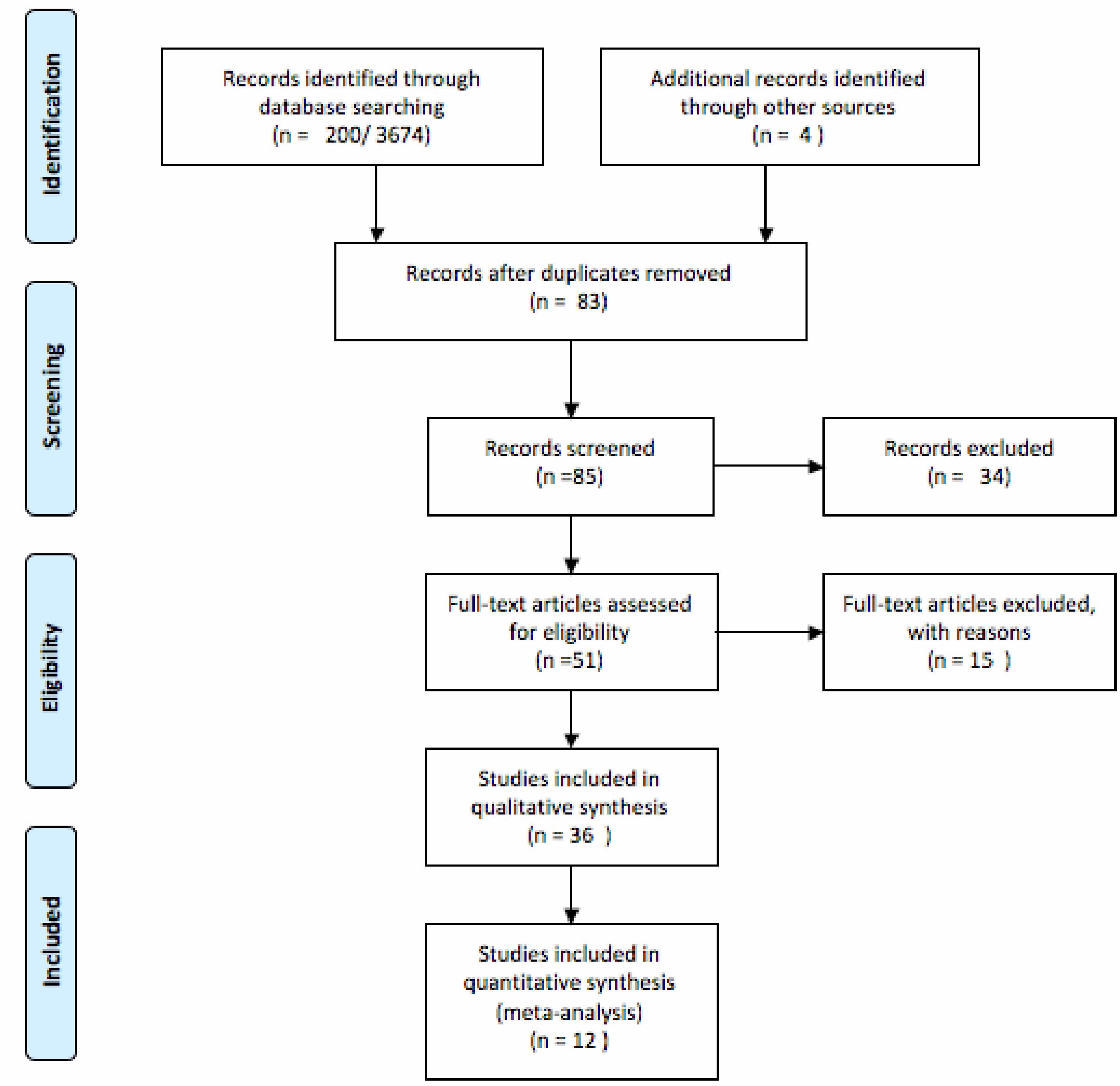

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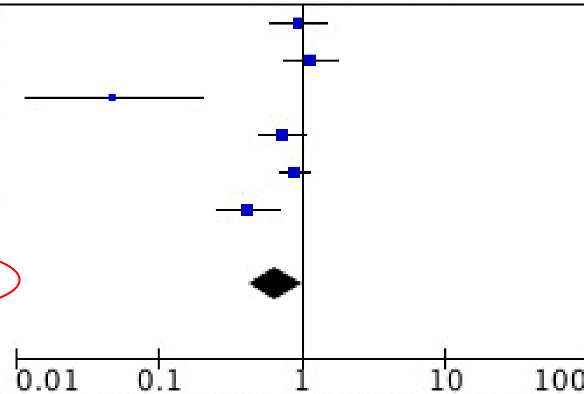
Topical repellents

Study or Subgroup	Repellent Events	Repellent Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Chen-Hussey 2012	36	88508	38	87516	17.9%	0.94 [0.59, 1.48]
Deressa 2010	44	19192	36	18180	18.2%	1.16 [0.75, 1.80]
Hill 2007a	2	30824	40	29872	6.3%	0.05 [0.01, 0.20]
McCready 2001	48	8082	66	8064	19.3%	0.72 [0.50, 1.05]
Onyango 2013	122	101504	138	101660	21.2%	0.89 [0.69, 1.13]
Rowland 2004	23	14832	47	12720	17.2%	0.42 [0.25, 0.69]
Total (95% CI)		**262942**		**258012**	**100.0%**	**0.66 [0.44, 1.00]**
Total events	275		365			

Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 26.44$, df = 5 ($P < 0.0001$); $I^2 = 81\%$

Test for overall effect: Z = 1.94 (P = 0.05)



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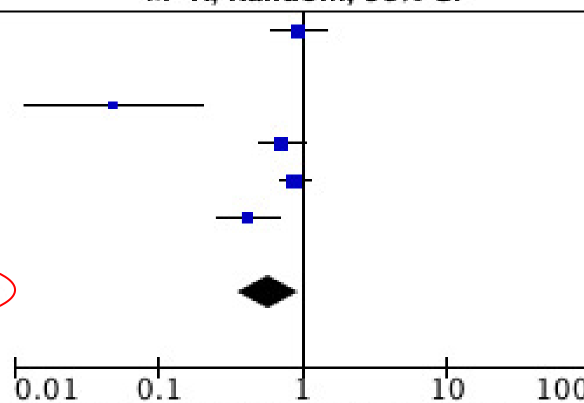
Rowland 2004	23	14832	47	12720	21.1%	0.42 [0.25, 0.69]
Total (95% CI)		**243750**		**239832**	**100.0%**	**0.58 [0.35, 0.94]**
Total events	231		329			

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 23.21$, df = 4 ($P = 0.0001$); $I^2 = 83\%$

Test for overall effect: Z = 2.23 (P = 0.03)



TOPICAL REPELLENTS							
Trial	**Intervention**	**EPI effect size (odds ratio)**	**VEC effect size**	**Primary Vector**	**Vector feeding behaviour**	**Compliance**	**Other points**
Chen Hussey 2012 [11]	15% DEET lotion in addition to Permanet 2.0 LLINs	0.94 (0.59-1.48)	98.9% protection for 5 hours in field tests	*Anopheles dirus, An. minimus* and *An. maculatus*	20 – 50% of biting before 10 pm [12]	About 50%	
Deressa 2010 [13]	Buzz off repellent plus Permanet LLIN	1.16 (0.75 – 1.80)	> 80% effective against *An. gambiae* for 8 hours in laboratory tests	*An. arabiensis*	70% before 10pm [14]	No measured	Repellent arm had more malaria to begin with. Effect size calculated by study accounting for imbalance was 0.57 (0.35 – 0.94) p=0.028
Hill 2007a [15]	30% PMD lotion in addition to 25mg/m² deltamethrin impregnated bednet.	0.05 (0.01-0.20)	Repellent provided 97% protection from *An. darlingi* for 4 hours [16]	*An. darlingi*	48% of biting before 21.00hrs [17]	>90% (per protocol analysis)	
McGready 2001 [18]	Repellent lotion containing 20% DEET and thanaka (*Limonia acidissima*)	0.72 (0.50 – 1.05)	repellent provided 65% reduction in exposure to *An. minimus* and 85% reduction in exposure to *An maculatus* [19]	*An. minimus* and *An. maculatus*	*An. minimus* 22% and *An. maculatus* 62% before bed time	Compliance actively detected at 84.6%	
Onyango 2013 Not published	15% DEET lotion in addition to Olyset LLINs	0.89 (0.69 – 1.13)	repellent prevented >80% bites from *An. arabiensis* over 4 hours	*An. arabiensis*	30% before 10pm	>90% (per protocol analysis) but application not adequately measured	
Rowland 2004 [20]	20% DEET and 0.5% permethrin soap	0.42 (0.25 - 0.69)	*An. stephensi* and *An. culicifacies* density– repellent prevented 100% bites over the whole night	100% effective	80% of anopheline biting before midnight	Self-reported compliance >95%	

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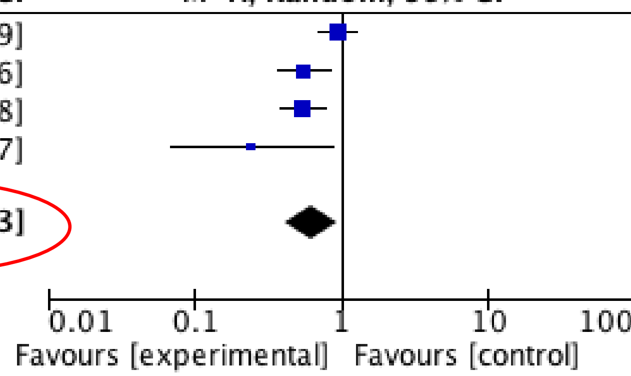
PERMETHRIN TREATED CLOTHING							
Trial	**Intervention**	**EPI effect size (odds ratio)**	**VEC effect size**	**Primary Vector**	**Vector feeding behaviour**	**Compliance**	**Other points**
Eamsila 1994 [21]	Treated uniform with 2g Permethrin per uniform once every 6 months	0.96 (0.71 – 1.29)	100% effective for 3 months, 84.45% effective up to 6 months	*An. dirus*	Not measured	100% compliance although it is not known if the uniforms were worn "correctly"	
Kimani 2006 [22]	Clothing treated with 0.37% Permethrin – retreated every three weeks	0.56 (0.36 - 0.86)	41% reduction in blood fed mosquitoes in users' houses and 41% increase in fed mosquitoes in non-users' houses	*An. arabiensis*	Not measured	not mentioned (assume all clothes were treated)	Reported odds of malaria in treatment group is 0.314 p=0.0002
Rowland1999 [20]	1g/m2 permethrin treated chaddars	0.55(0.38 – 0.78)	reduced feeding success of An. nigerrimus, An stephensi and An. subpictus by 0-60%	An stephensi	80% of anopheline biting before midnight	not measured	
Soto 1995 [23]	Treated uniform with 600-712mg/m2 permethrin	0.24(0.07-0.87)	not measured	An. darlingi	not measured	not measured	

	Experimental		Control			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Eamsila 1994	68	5976	118	9936	33.1%	0.96 [0.71, 1.29]
Kimani 2006	34	1080	60	1092	27.8%	0.56 [0.36, 0.86]
Rowland 1999	51	7008	82	6192	31.0%	0.55 [0.38, 0.78]
Soto 1995	3	344	12	344	8.1%	0.24 [0.07, 0.87]
Total (95% CI)		**14408**		**17564**	**100.0%**	**0.62 [0.41, 0.93]**
Total events	156		272			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 9.78$, df = 3 (P = 0.02); $I^2 = 69\%$
Test for overall effect: Z = 2.31 (P = 0.02)

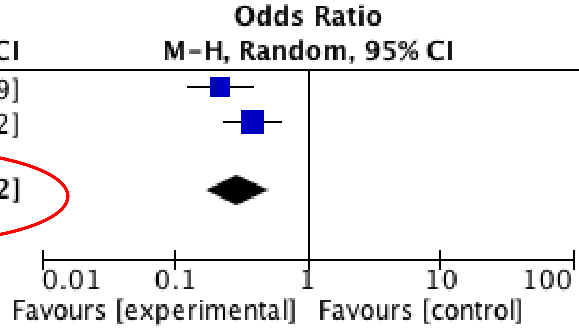
Odds Ratio
M-H, Random, 95% CI



SPATIALLY ACTIVE VOLATILE PYRETHROIDS						
Trial	**Intervention**	**EPI effect size (odds ratio)**	**VEC effect size**	**Primary Vector**	**Vector feeding behaviour**	**Compliance**
Syafruddin 2012 [7]	4 x 0.00975 metofluthrin coils per house per night	0.39 (0.24-0.62)	32.9% reduction in mosquito landings by HLC	*An. sundaicus*	33% of biting before 10pm [8]	Nightly
Hill 2007 [9]	2 x 0.03 %transfluthrin coils per house per night	0.22 (0.13-0.39)	88% reduction in indoor mosquito densities by CDCLT	*An. sinensis*	47% of biting before 10pm [10]	>90%

Study or Subgroup	Volatile pyrethroid coils Events	Volatile pyrethroid coils Total	No Intervention Events	No Intervention Total	Weight	Odds Ratio M-H, Random, 95% CI
Hill 2007	15	36152	68	36424	46.3%	0.22 [0.13, 0.39]
Syafruddin 2012	25	1381	59	1296	53.7%	0.39 [0.24, 0.62]
Total (95% CI)		**37533**		**37720**	**100.0%**	**0.30 [0.17, 0.52]**
Total events	40		127			

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 2.22$, df = 1 (P = 0.14); $I^2 = 55\%$
Test for overall effect: Z = 4.35 (P < 0.0001)



Repellency is used as a general term to refer to a range of insect behaviours induced by chemicals that result in a reduction in human-vector contact.

1. movement away from a chemical stimulus
2. interference with host detection (attraction-inhibition)
3. interference with feeding response
4. incapacitation

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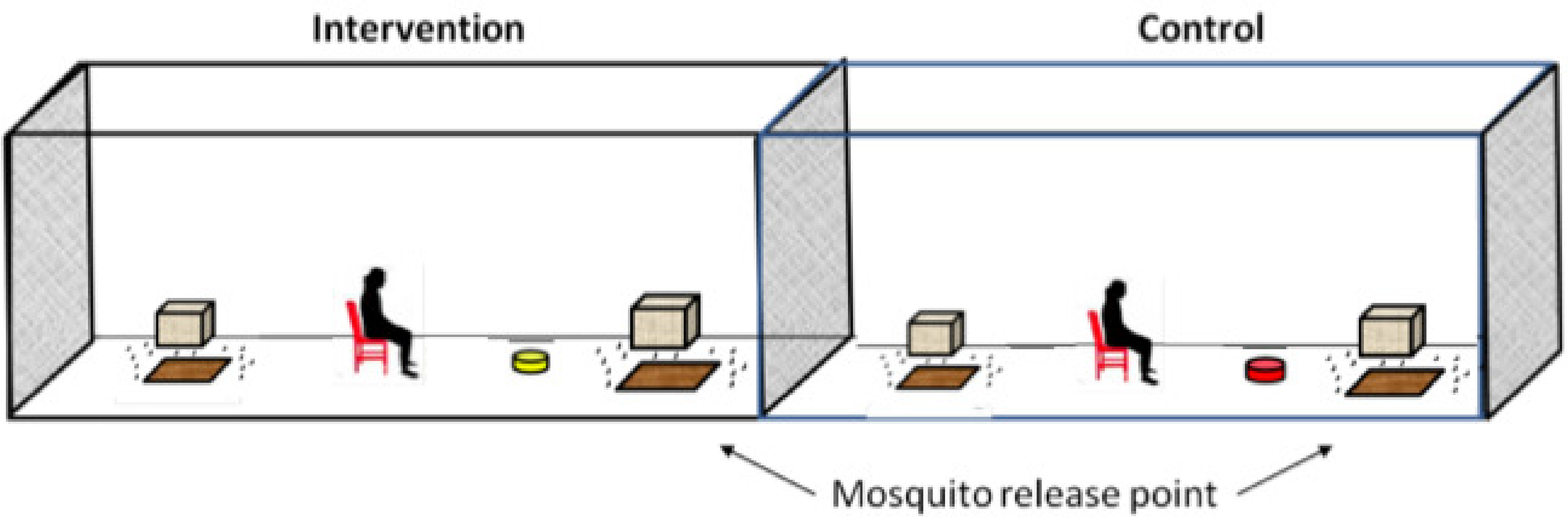
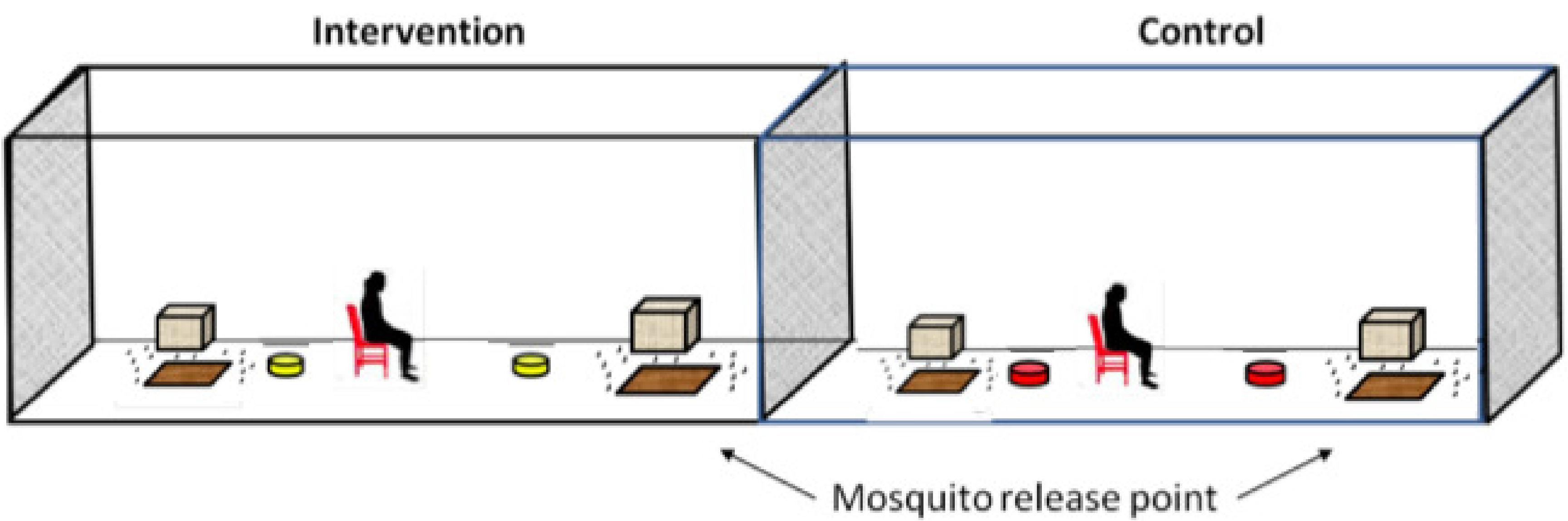
POINT SOURCE

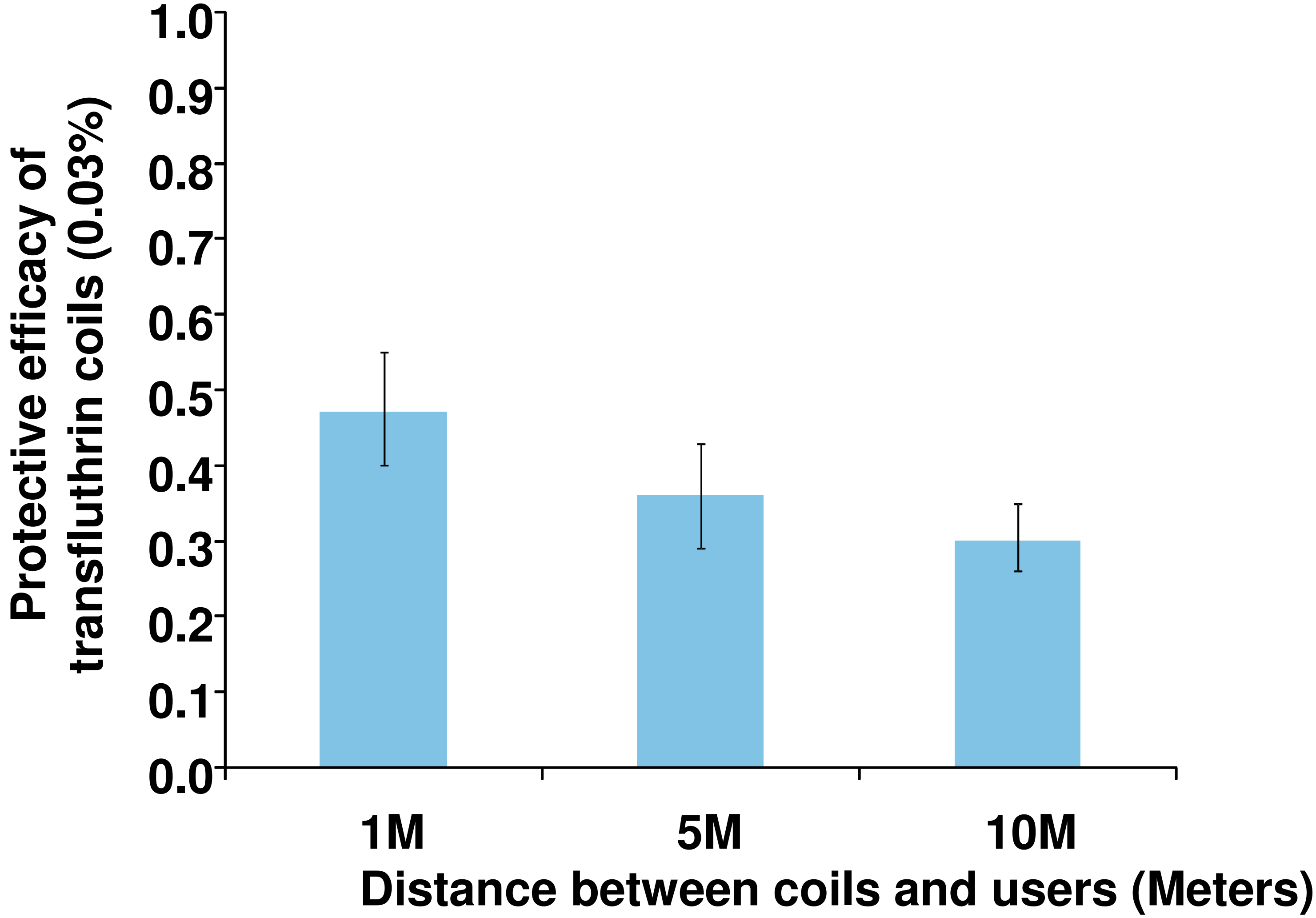


BUBBLE



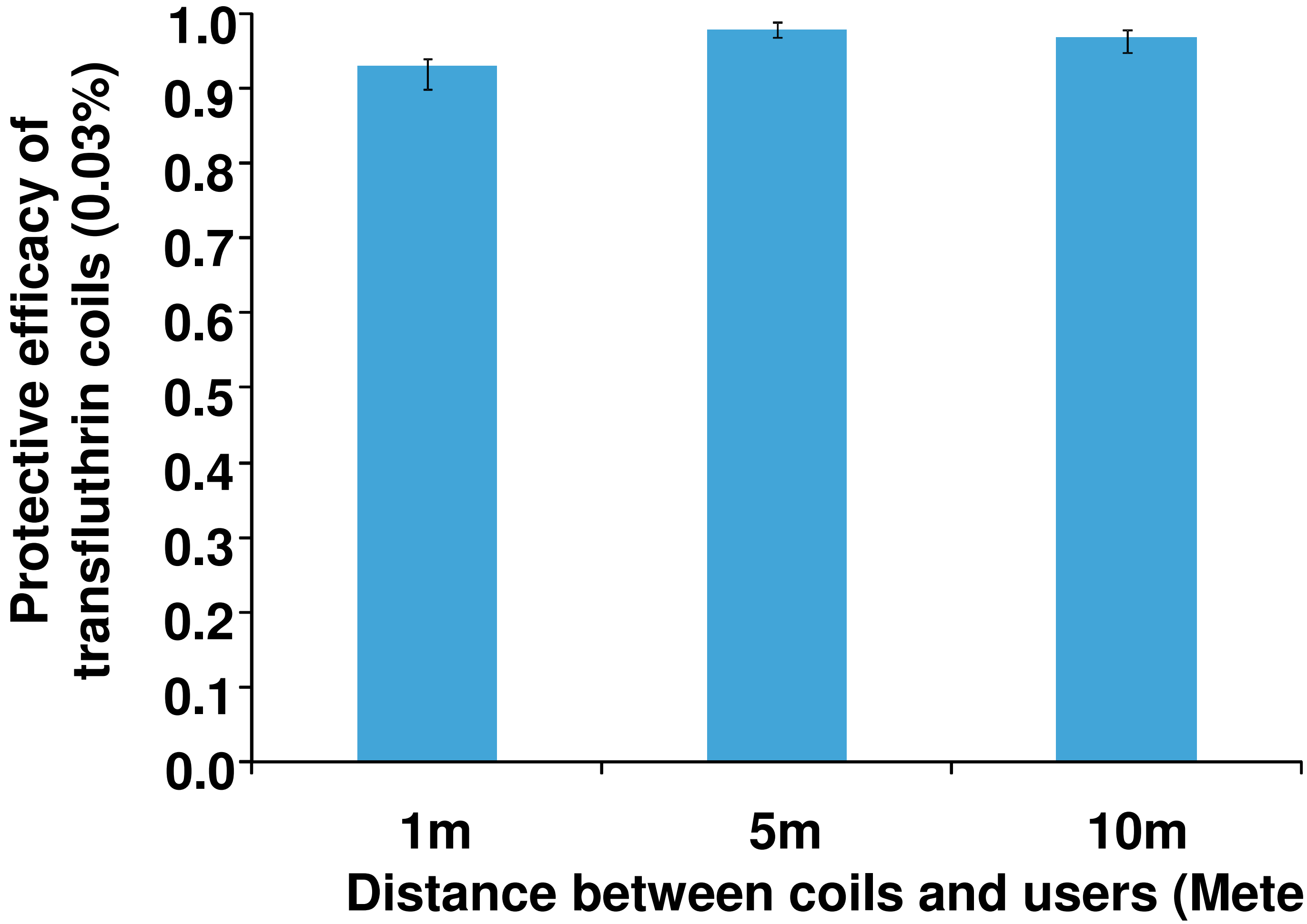
Transfluthrin coil as a "point source"

Point source reduced *Anopheles gambiae* s.s. bites to between 30% and 47% up to 10 metres from the source

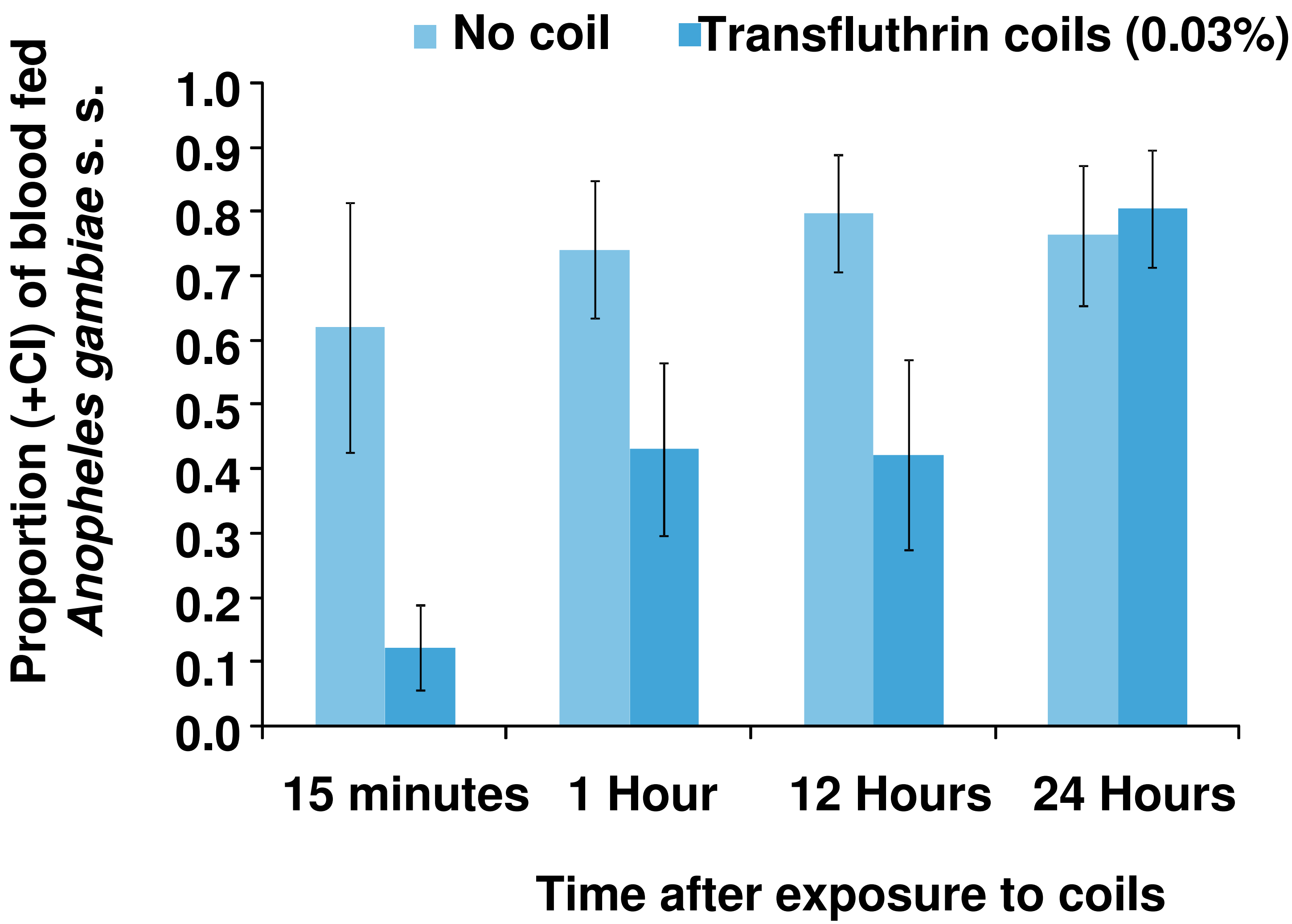


Transfluthrin coil as a "bubble"

Bubble effect reduced *Anopheles gambiae* s. s. bites by more than 90% up to 10m from the source



Proportion and 95% CI of *Anopheles gambiae* s. s. mosquitoes that fed after exposure to gold standard mosquito coils



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SHORT REPORT Open Access

Spatial repellency of transfluthrin-treated hessian strips against laboratory-reared *Anopheles arabiensis* mosquitoes in a semi-field tunnel cage

Sheila B Ogoma[1,2*], Hassan Ngonyani[1], Emmanuel T Simfukwe[1], Anthony Mseka[1], Jason Moore[1,2] and Gerry F Killeen[1,3]

Ogoma *et al. Parasites & Vectors* 2012, **5**:54
http://www.parasitesandvectors.com/content/5/1/54

ROLL BACK MALARIA

Functional agonism of insect odorant receptor ion channels

Patrick L. Jones[a,1], Gregory M. Pask[a,1], David C. Rinker[b], and Laurence J. Zwiebel[a,b,c,2]

BEHAVIOURAL NEUROBIOLOGY

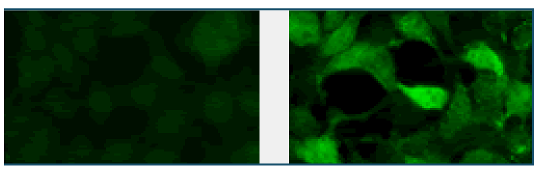
The treacherous scent of a human

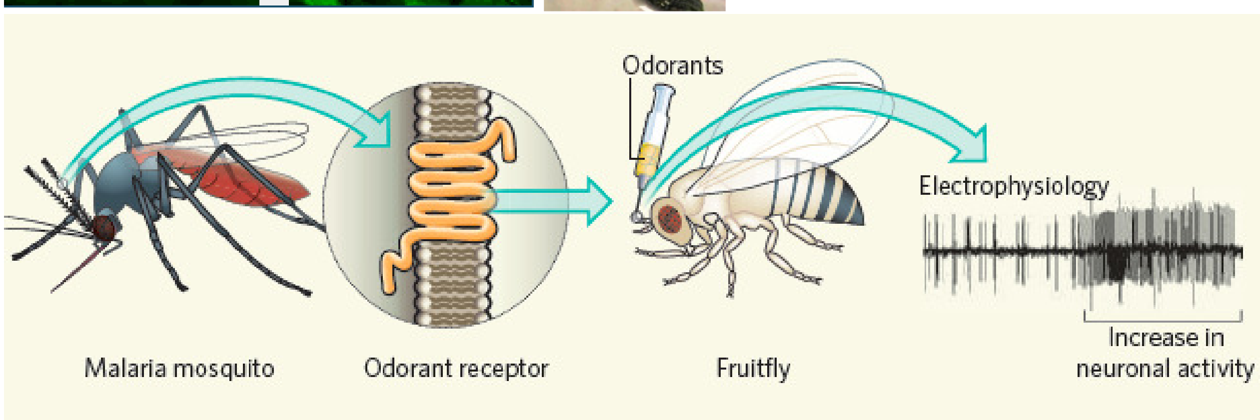
Walter S. Leal

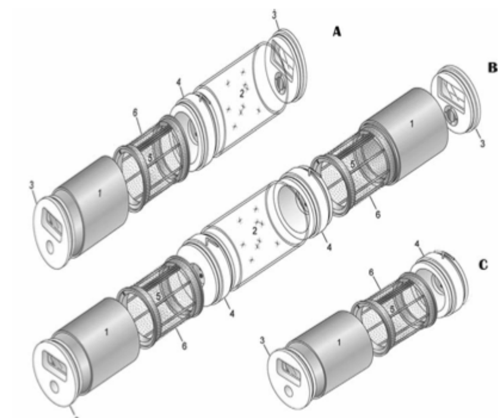
Mosquitoes' odorant receptors help the insects to find humans and, inadvertently, to transmit malaria. The identification of the odorants that bind to these receptors opens up ways of reducing mosquito biting.

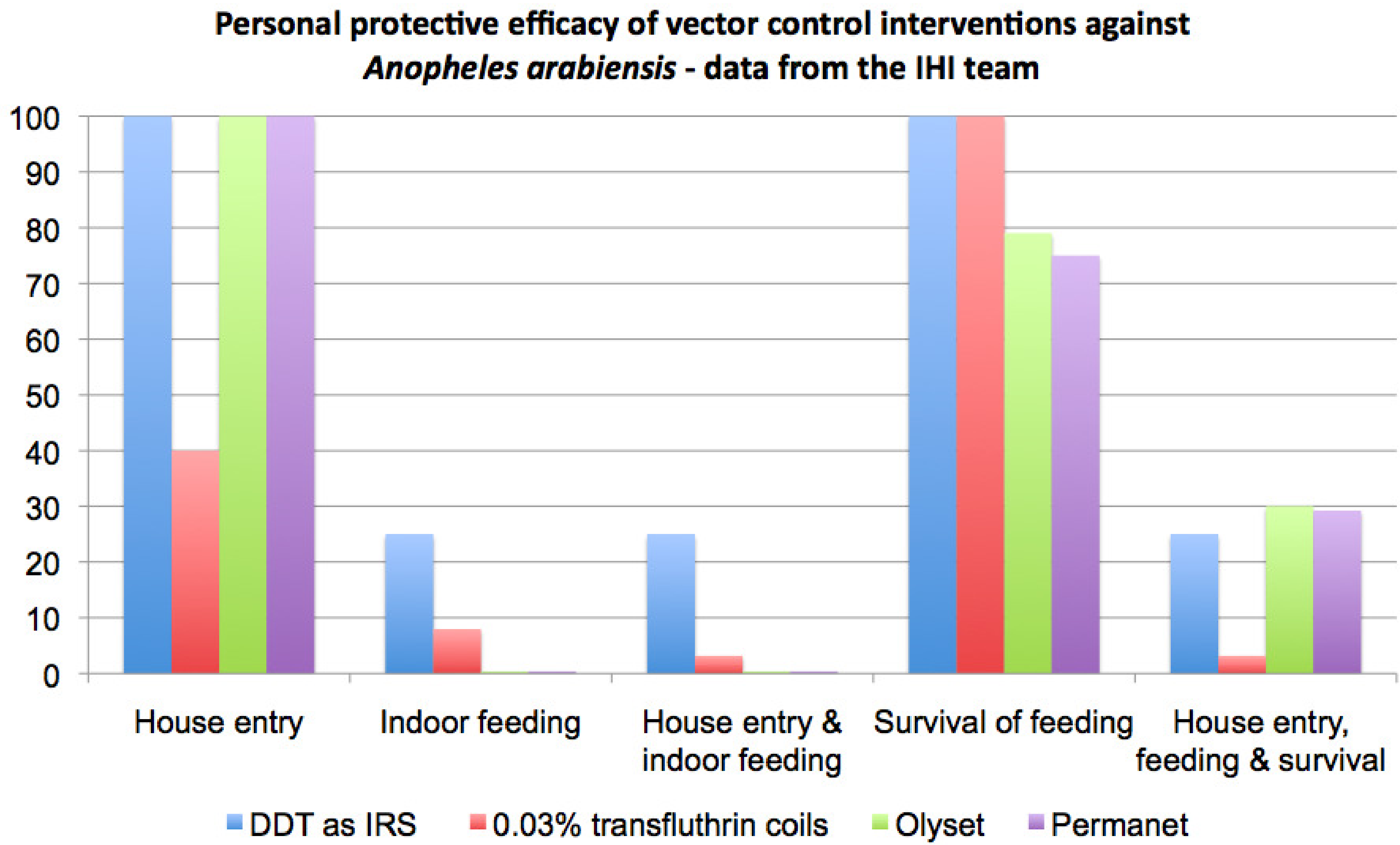
Ultra-prolonged activation of CO_2-sensing neurons disorients mosquitoes

Stephanie Lynn Turner[1]*, Nan Li[2]*, Tom Guda[3], John Githure[3], Ring T. Cardé[2] & Anandasankar Ray[1,2]









Okumu *et al* Comparative evaluation of combinations of long lasting insecticidal nets and indoor residual spraying, relative to the use of either method alone, for malaria vector control in an area dominated by *Anopheles arabiensis. Accepted- Malaria Journal*

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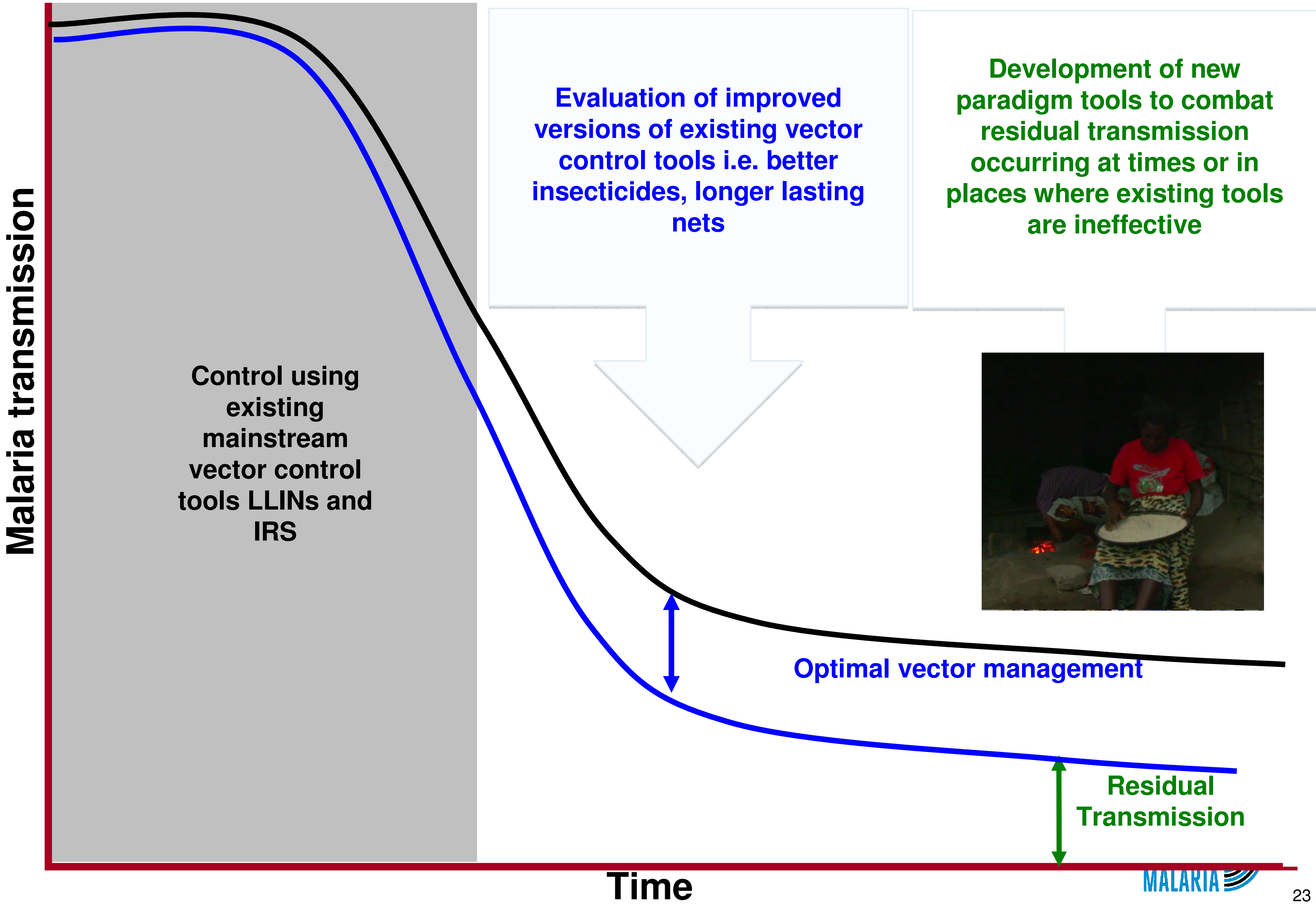

Malaria transmission
Control using existing mainstream vector control tools LLINs and IRS
Evaluation of improved versions of existing vector control tools i.e. better insecticides, longer lasting nets
Development of new paradigm tools to combat residual transmission occurring at times or in places where existing tools are ineffective
Optimal vector management
Residual Transmission
Time


MOSQUITO
REPELLENT

Can you have community protection without killing mosquitoes?

Source reduction of mosquito larval habitats has unexpected consequences on malaria transmission

Weidong Gu*†, James L. Regens‡, John C. Beier§, and Robert J. Novak*

*Illinois Natural History Survey, Champaign, IL 61820; ‡Department of Occupational and Environmental Health, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104; and §Department of Epidemiology and Public Health, University of Miami, Miami, FL 33177

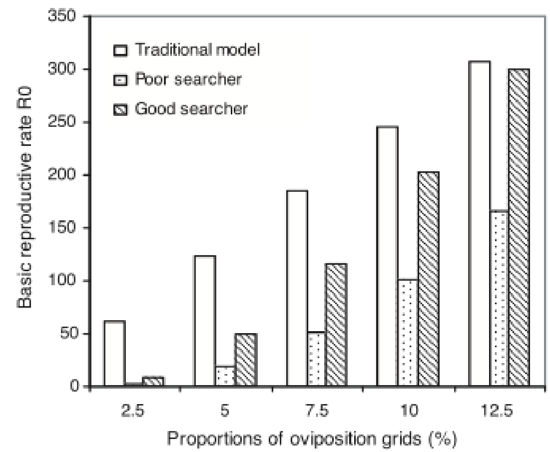
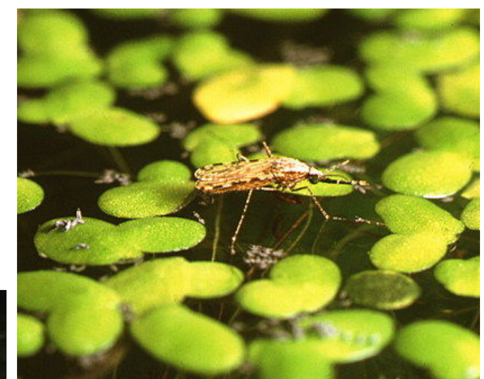


Fig. 1. Basic reproductive rate R_0 predicted by the traditional model, which assumes a fixed (3 days) duration of the gonotrophic cycle, and our behavior model of the gonotrophic cycle for various scenarios of proportions of oviposition grids and flight ability.

Table 1. Duration (in days) of the gonotrophic cycle as a function of the availability of aquatic habitats and the flight ability of mosquitoes

Proportion of oviposition grids in the landscape, %	Duration of gonotrophic cycle	
	Poor searcher (250 m/day)	Good searcher (500 m/day)
2.5	13.6	7.7
5	7.6	4.7
7.5	5.6	3.8
10	4.7	3.3
12.5	4.1	3.0



Lifetime fecundity

Host availability

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Why not use repellents in situation-appropriate format for public health?

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