

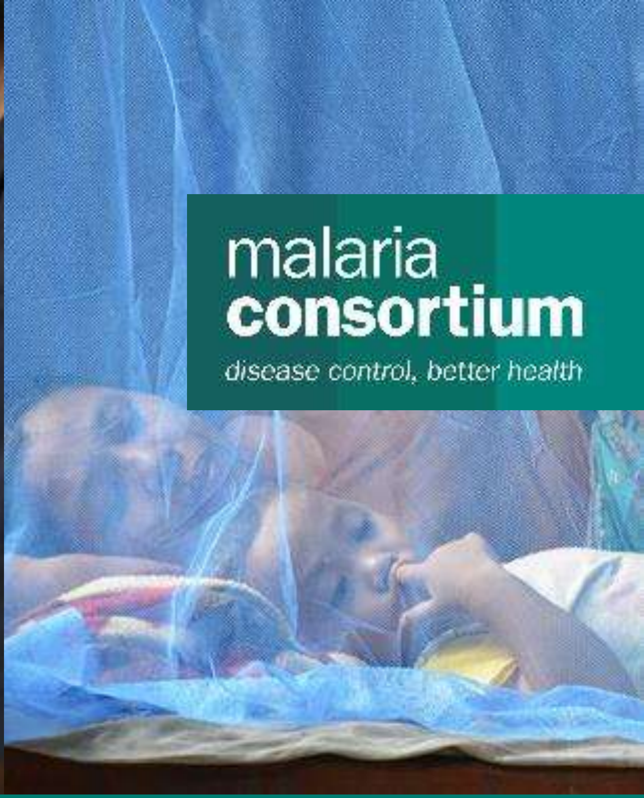

Overview of integrated vector management (IVM), summary of previous dengue vector control trials in Cambodia

John Hustedt

Vector control tools tested in Cambodia

Tool Used	When	Where	Results/Challenges	Ref
Temephos	Ongoing distribution	Country wide	Larval Resistance	Polson et al (2001) Khun & Manderson (2007)
Thermal Fogging	Ongoing	OD staff Private Sector	Resistance to Permethrin/Deltamet hrin	
Mesocyclops	2003-2004	Kratie	Low acceptance/low efficacy	
Treated Covers	2008	Kampong Cham	Short efficacy on medium term	Seng *et al* (2008)
Guppy Fish	2008	Kampong Speu	79% less larvae in targeted containers	Seng et al (2008)
	2010/2011	Kampong Cham	CI/PPP in intervention significantly lower than in control	WHO/ADB (2013)
Bti	2007 2016	Phnom Penh	Reduction in pupae for 10-13 weeks	Setha et al (2007) Setha et al (2016)
Pyriproxifen	2006 2008	Phnom Penh Phnom Penh	IE > 95% IE > 80% for 34 weeks	Seng et al (2006) Seng et al (2008)

Temephos (Abate)

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Abate distribution and dengue control in rural Cambodia

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Available online 16 January 2007

Temephos (Abate)

Background

- Abate distribution has been conducted yearly since mid 1990s, with financial support for the larvicide and health education materials provided by the Cambodian Ministry of Health, World Health Organization (WHO), the International Red Cross, and the World Bank.
- The Ministry of Health spends around US$1 million per annum to purchase 200 metric tonnes of Abate.
- In 2002, WHO and the World Bank also provided US$ 150,000 and 250,000, respectively, to meet the operational costs of distribution, such as transportation, per diem for distributors and the cost of packaging Abate into small plastic bags.
- In 2003, Abate was distributed to select areas in 15 out of 22 dengue endemic provinces in the country, based on the prevalence of the disease identified by monthly surveillance reports.

Temephos (Abate)

Challenges

- Coverage varied significantly, based on the commitment of distributors.
- Difficulties in measuring the container capacity correctly and incorrect quantities of Abate being placed in containers.
- Where Abate was introduced with minimal health education, some householders refused to accept it, or removed the bag of Abate from their water containers.
- Limited understanding of the duration of its effectiveness as a larvicide and less understanding and adherence to other control activities.
- Water jars were positive with larvae in both rainy and dry seasons, although Abate was applied only in the rainy season.
- Development of insecticide resistance

Temephos (Abate)

Conclusions

- Control strategies emphasizing the use of Abate ***should be reconsidered***.
- In total, almost US$ 1.4 million is currently expended on the distribution of Abate, which could be redirected, at least in part, for other preventive activities such as the production of appropriate, effective and sustained health education and promotion as a health centre outreach activity.

Mesocyclops

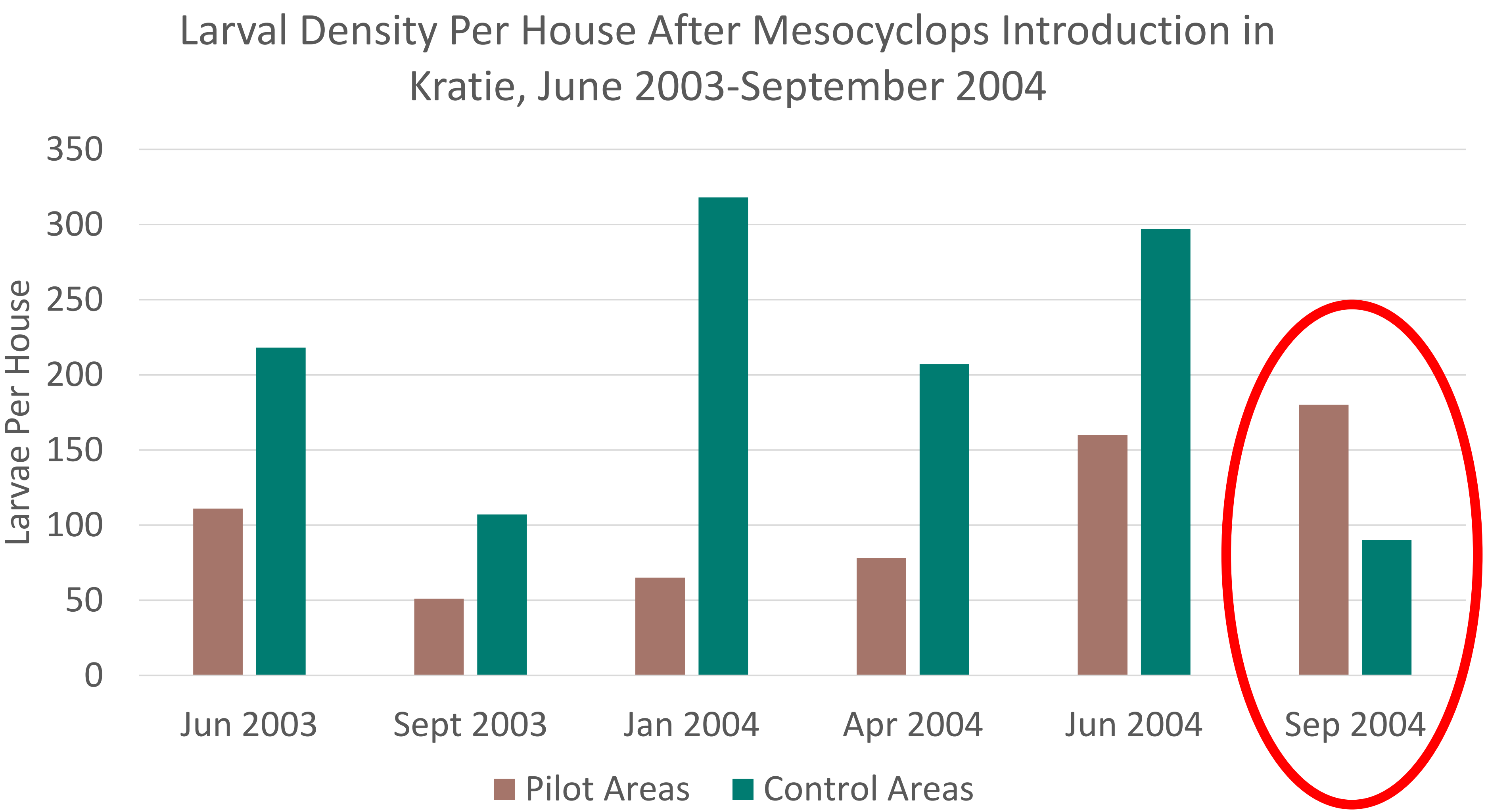
Mesocyclops

- Following the success of *Mesocyclops* (a genus of copepod crustaceans) programs in locally eliminating *Aedes* mosquitoes In Vietnam, the Cambodian NDCP implemented a two year *Mesocyclops* project in Kratie province.

- *Mesocyclops* from the local water sources had various parasites, and colonising them parasite-free requires special training beyond what is possible in most rural Cambodian villages.

- People did not accept *Mesocyclops* to the same extent as other interventions that were provided by the NDCP such as temephos.

Mesocyclops



Insecticide Treated Jar Covers

Insecticide Treated Jar Covers

Vol. 33, no. 2 *Journal of Vector Ecology* 333

The effect of long-lasting insecticidal water container covers on field populations of *Aedes aegypti* (L.) mosquitoes in Cambodia

Chang Moh Seng[1]✉, To Setha[2], Joshua Nealon[1], Ngan Chantha[2], Doung Socheat[2], and Michael B. Nathan[3]

[1]*World Health Organization Cambodia. #177-179, Pasteur Street (51), Phnom Penh, Cambodia*
[2]*National Centre of Parasitology, Entomology and Malaria Control, Ministry of Health, Phnom Penh, Cambodia*
[3]*Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland*

Received 2 April 2008; Accepted 31 July 2008

Insecticide Treated Jar Covers (Seng et al. 2008)

- Despite correct high utilization rates (88%), cost of $1.20 is prohibitive to most rural Cambodians
- Container cover not 100% insect-proof due to incorrect closure allowing mosquito entry and exit
- Harsh outdoor tropical environment degrade fabric & netting of water jar covers; more improvements are needed
- Potential insecticide resistance development → safe alternatives to pyrethroids
- What is the strategy for the “last mile”?

Insecticide Treated Jar Covers (Seng et al. 2008)

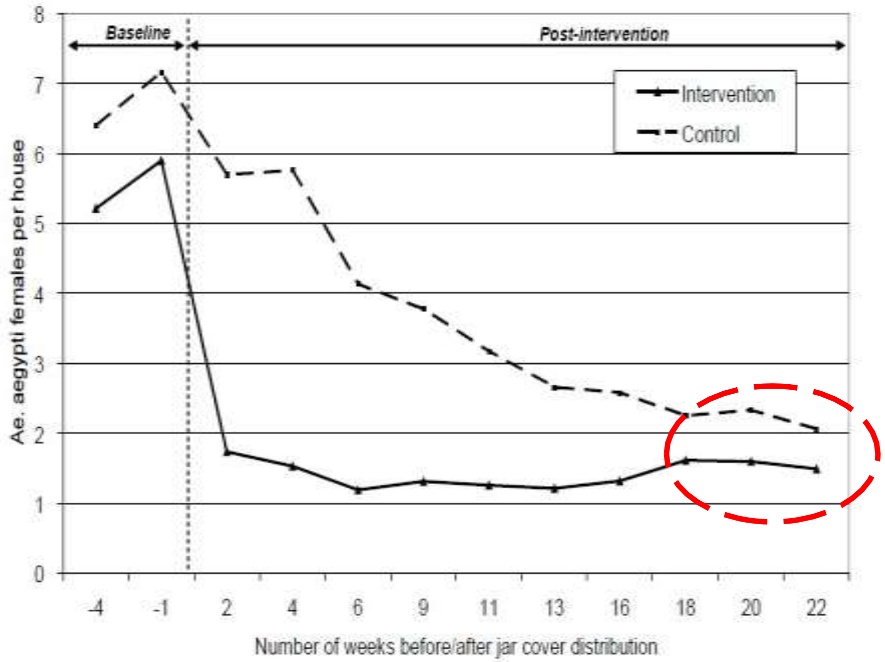


Figure 1. Mean number of indoor resting female *Ae. aegypti* per house in the intervention and control areas.

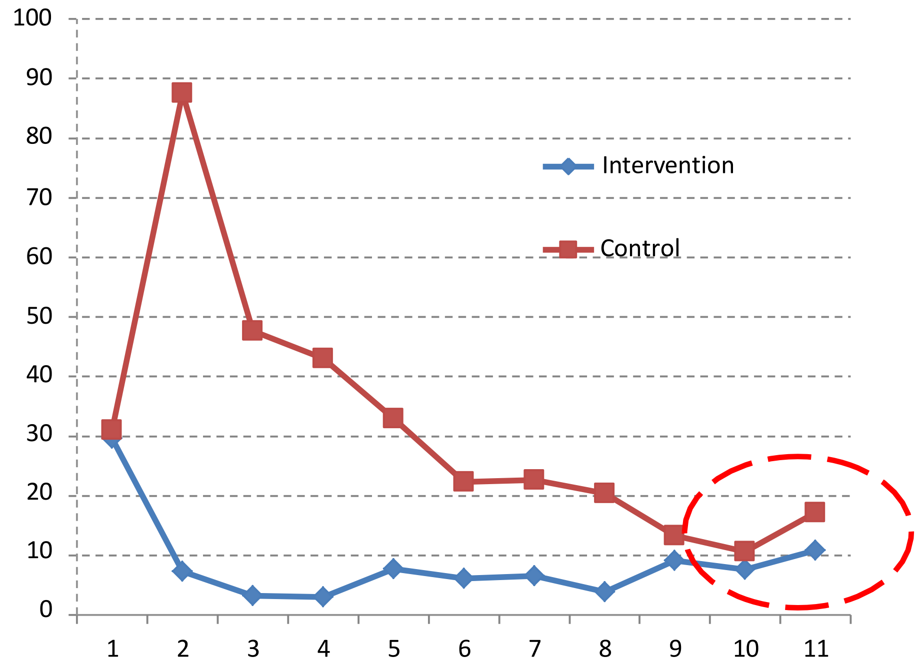


Figure 2: Mean *Aedes* pupae per house

Guppy Fish

Guppy Fish (Seng et al. 2008)

- One year after project commencement, 56.9% of eligible containers contained guppies and there was a 79.0% reduction in *Aedes* infestation in the intervention community compared with the control.
- Smaller or discarded containers unsuitable for guppy distribution in the intervention area also had 51% less infestation than those in the control area, suggesting a "community-wide" protective effect.

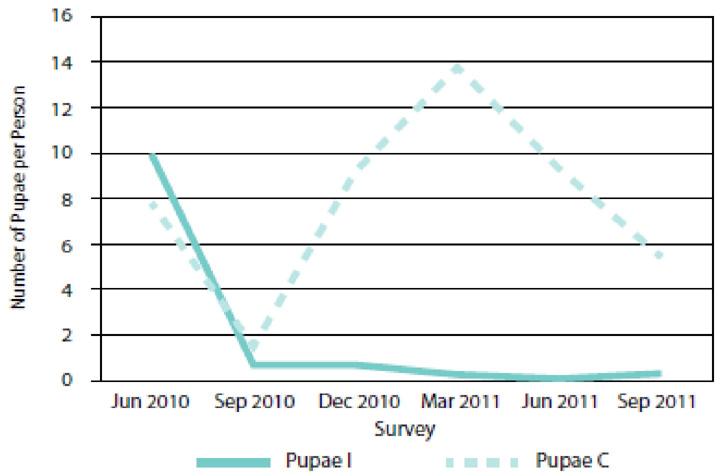
Table 4. The house, container, and Breteau indices of the intervention and control areas of this study one year after project implementation. "n" refers to either number of houses ([a]) or number of containers ([b]). "No. positive" refers to the number of houses ([c]) or containers ([d]).

Area	House Index			Container Index			Breteau Index		
	n[a]	No. positive[c]	Index	n[b]	No. positive[d]	Index	n[a]	No. positive[d]	Index
Intervention	249	112	**45.0**	1626	179	**11.0**	249	179	**71.9**
Control	65	61	**93.8**	541	255	**47.1**	65	255	**392.3**

Guppy Fish (WHO, 2013)

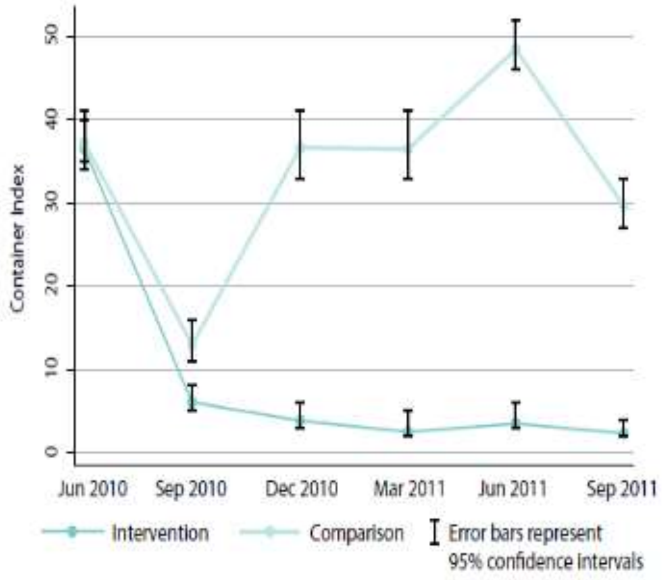
- The project resulted in a decline in the number of mosquito larvae present in three key water containers (jars, cement tanks, and drums).
- Scale-up of the low-cost intervention ***is recommended in Cambodia and Lao***
- Accepted well by community

Figure 20 Mean Number of *Aedes aegypti* Pupae per Person at the Time of the Survey, Cambodia



Pupae I = pupae in intervention villages, Pupae C = pupae in comparison villages.
Source: HLSP (2012).

Figure 18 Percentage of Water Containers with *Aedes aegypti* Larvae or Pupae (Container Index), by Village and Survey Time Point, Cambodia



Source: HLSP (2012).

Bacillus Thuringiensis Israelensis (Bti)

Bti (Setha et al, 2007)

EFFICACY OF *BACILLUS THURINGIENSIS ISRAELENSIS*, VECTOBAC® WG AND DT, FORMULATIONS AGAINST DENGUE MOSQUITO VECTORS IN CEMENT POTABLE WATER JARS IN CAMBODIA

To Setha, Ngan Chantha and Doung Socheat

National Malaria Center (CNM), Center for Entomology, Parasitology and Malaria Control, Phnom Penh, Cambodia

Bti (Setha et al, 2007)

- The VectoBac treatments significantly reduced the pupae numbers for a minimum of 3 months in the river water and 2.5 months in the well water.
- In the rain water, the pupae densities in the VectoBac WG® and DT® treated jars were not significantly different from the untreated jars.
- It was also observed that VectoBac WG® and DT® were target specific, without any adverse effects on aquatic predatory insects common in well and rain water.

Bti (Setha et al, 2007)

Table 2
Mean number of pupae collected from cement jars per week from 12 June to 6 September 2004 and successfully emerged into *Ae. aegypti* adults.

Water type	Treatment	Mean no. of *Ae. aegypti* pupae collected per week		
		1st month post-treatment $\chi \pm$ SE (p value)[a]	2nd month post-treatment $\chi \pm$ SE (p value)[a]	3rd month post-treatment $\chi \pm$ SE (p value)[a]
River water	VectoBac WG	2.0 ± 1.41 (p=0.023)	1.25 ± 0.95 (p=0.066)	1.75 ± 1.75 (p=0.008)
	VectoBac DT	2.5 ± 2.50 (p=0.025)	2.25 ± 1.65 (p=0.072)	1.75 ± 0.25 (p=0.008)
	UTC	45.50 ± 14.22	39.75 ± 17.14	56.75 ± 13.98
Well water	VectoBac WG	5.5 ± 5.17 (p=0.082)	0.5 ± 0.29 (p=0.013)	9.0 ± 2.86 (p=0.396)
	VectoBac DT	4.25 ± 4.25 (p=0.069)	5.00 ± 3.72 (p=0.051)	3.50 ± 1.94 (p=0.242)
	UTC	37.75 ± 14.56	23.25 ± 6.50	22.50 ± 14.51
Rain water	VectoBac WG	21.50 ± 19.84 (p=0.377)	6.25 ± 5.60 (p=0.626)	29.5 ± 29.5 (p=0.715)
	VectoBac DT	11.50 ± 7.24 (p=0.23)	1.50 ± 1.50 (p=0.095)	9.0 ± 8.03 (p=0.213)
	UTC	61.00 ± 36.35	9.75 ± 3.88	44.00 ± 23.82

[a] *T*-test was done to determine the significant difference between the respective populations in treated and untreated jars with each Bti formulation.

Bti (Setha et al. 2016)

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

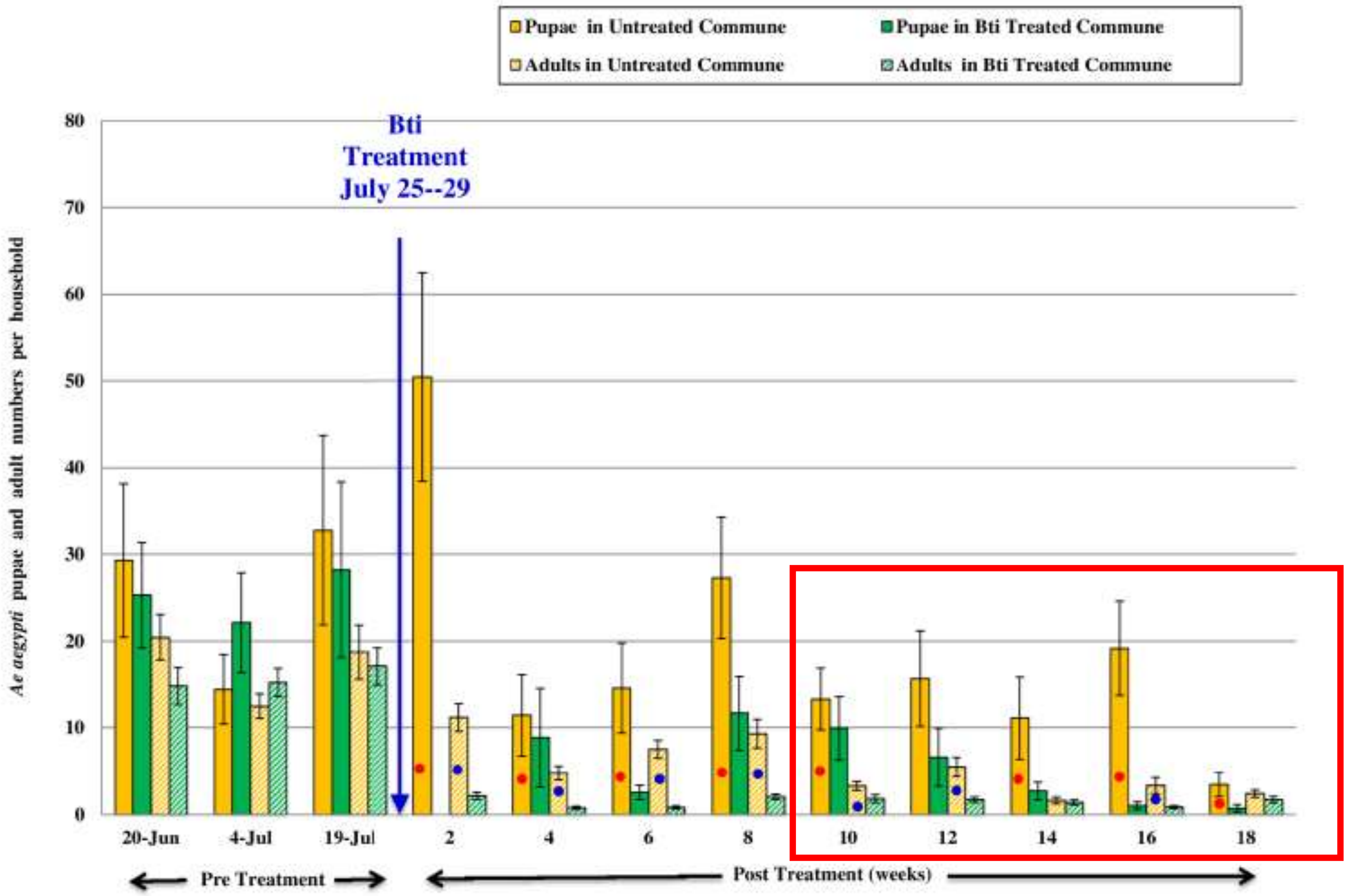
Bacterial Larvicide, *Bacillus thuringiensis israelensis* Strain AM 65-52 Water Dispersible Granule Formulation Impacts Both Dengue Vector, *Aedes aegypti* (L.) Population Density and Disease Transmission in Cambodia

To Setha[1☯*], Ngan Chantha[1†‡], Seleena Benjamin[2☯], Doung Socheat[1‡]

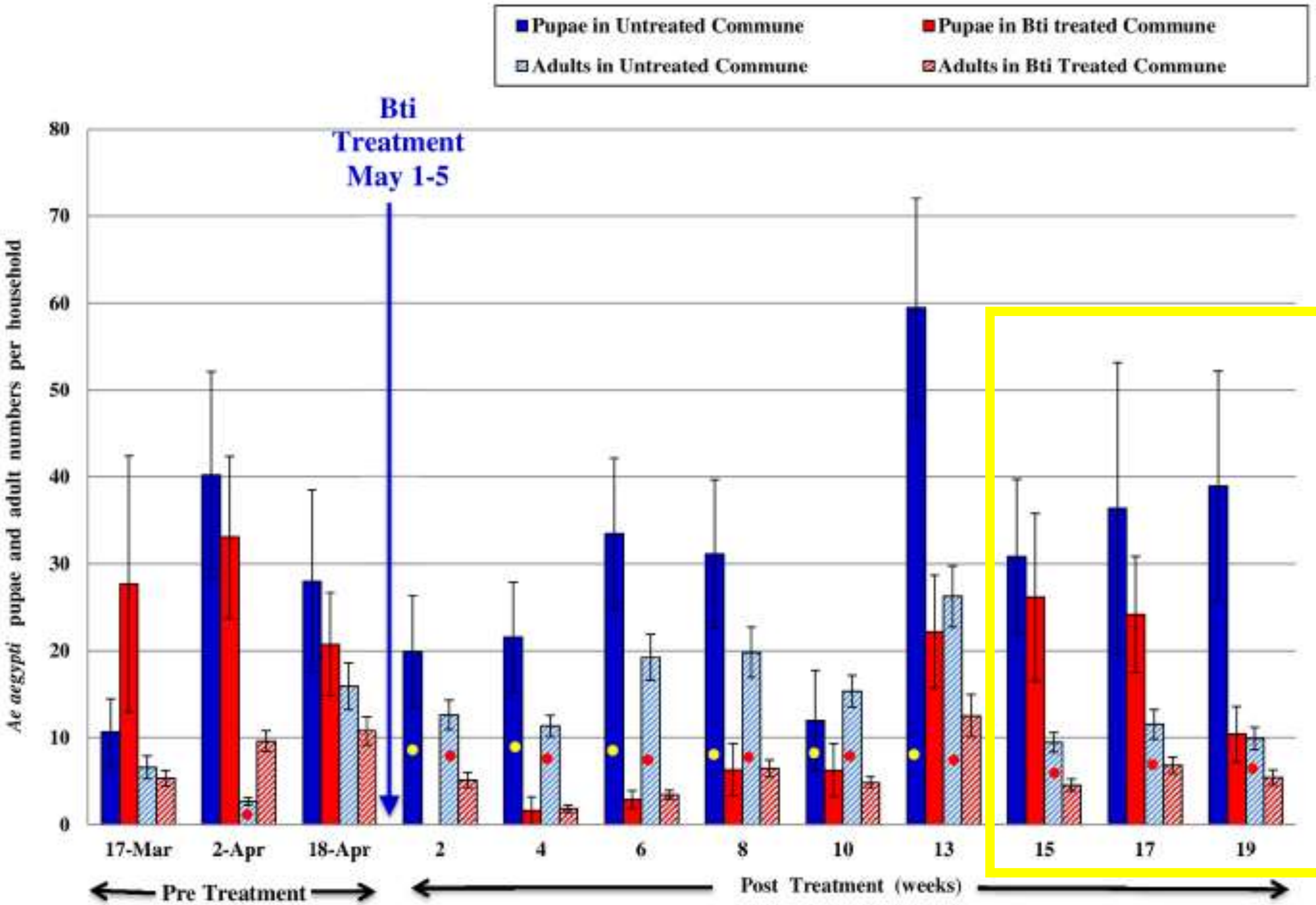
1 National Center for Parasitology, Entomology and Malaria Control, Ministry of Health, Phnom Penh, Cambodia, **2** Public Health, Valent BioSciences Corporation, Kuala Lumpur. Malaysia

Bti (Setha et al. 2016)

- Good supporting evidence that larviciding with Bti strain AM65-52 by a single dose of 8g per 1000 L in all in-use containers significantly suppresses *Aedes aegypti* pupae production and adult mosquitoes for a continuous **13 weeks** in the peak rainfall and vector season.

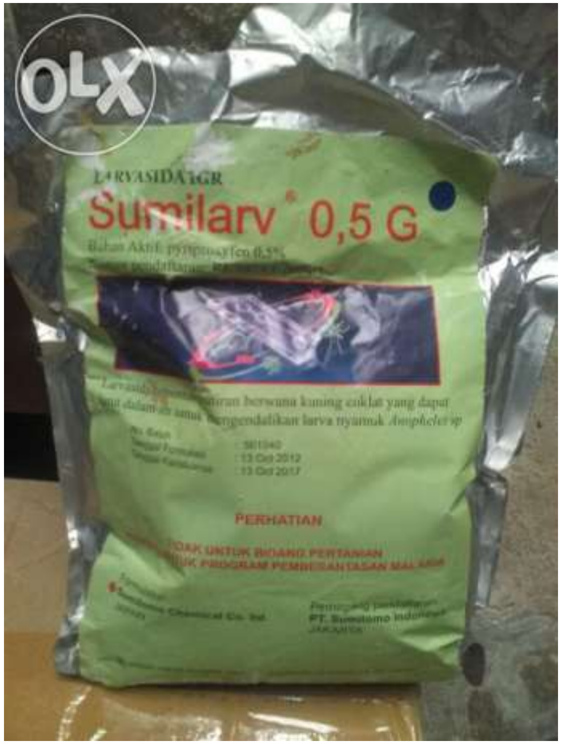


Pupae in Untreated Commune
Pupae in Bti Treated Commune
Adults in Untreated Commune
Adults in Bti Treated Commune
Bti Treatment July 25--29
Ae aegypti pupae and adult numbers per household
0
10
20
30
40
50
60
70
80
20-Jun
4-Jul
19-Jul
2
4
6
8
10
12
14
16
18
Pre Treatment
Post Treatment (weeks)



Pupae in Untreated Commune
Pupae in Bti treated Commune
Adults in Untreated Commune
Adults in Bti Treated Commune
Bti Treatment May 1-5
Ae aegypti pupae and adult numbers per household
0
10
20
30
40
50
60
70
80
17-Mar
2-Apr
18-Apr
2
4
6
8
10
13
15
17
19
Pre Treatment
Post Treatment (weeks)

Pyriproxyfen



Pyriproxyfen (Seng et al, 2008)

SIX MONTHS OF *AEDES AEGYPTI* CONTROL WITH A NOVEL CONTROLLED-RELEASE FORMULATION OF PYRIPROXYFEN IN DOMESTIC WATER STORAGE CONTAINERS IN CAMBODIA

Chang Moh Seng[1], To Setha[2], Joshua Nealon[1], Duong Socheat[2] and Michael B Nathan[3]

[1]World Health Organization, Phnom Penh; [2]Center of Parasitology, Entomology and Malaria Control, Ministry of Health, Phnom Penh, Cambodia; [3]Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland

Pyriproxyfen (Seng et al, 2008)

- This single treatment provided control of *Ae. aegypti* in water jars for the length of the main dengue transmission season in Cambodia that normally extends from May to November.
- The device floated on top of water and was easily scooped up by households
- No alteration of taste or other undesirable effects of the treatment were reported by householders.

Table 1

Inhibition of emergence (IE) of adult *Aedes aegypti* in domestic water storage jars, Phum Thmei, Cambodia, April-December, 2005.

	Weeks after treatment with pyriproxyfen[a]																	
	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	Total
Treated jars																			
No. of water jars	100	100	99	99	96	96	95	95	95	95	94	94	94	94	94	93	92	92	
No. of pupae collected	291	414	225	654	337	555	219	763	722	364	499	376	250	124	246	299	77	138	6,553
No. of viable adults emerged	291	1	0	5	1	0	0	2	13	11	13	48	0	22	14	30	10	27	488
Inhibition of emergence (%)	0.0	99.8	100.0	99.2	99.7	100.0	100.0	99.7	98.2	97.0	97.4	87.2	100.0	82.3	94.3	90.0	87.0	80.4	92.6
Control jars																			
No. of water jars	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	
No. of pupae collected	51	206	36	129	47	137	53	135	225	231	18	86	36	35	149	86	39	47	1,746
No. of viable adults emerged	50	199	36	126	46	135	53	132	223	231	18	83	35	35	146	85	39	47	1,719
Inhibition of emergence (%)	2	3.4	0	2.3	2.1	1.5	0	2.2	0.8	0	0	3.5	3.5	0	2	1.1	0	0	1.5

[a]Week 0 was a pre-treatment assessment.

Thermal Fogging

- No published data on efficacy or susceptibility of mosquitoes
- Impact on mosquito susceptibility from use by public and private sectors



Vector control tools tested in Cambodia

Tool Used	When	Where	Results/Challenges	Ref
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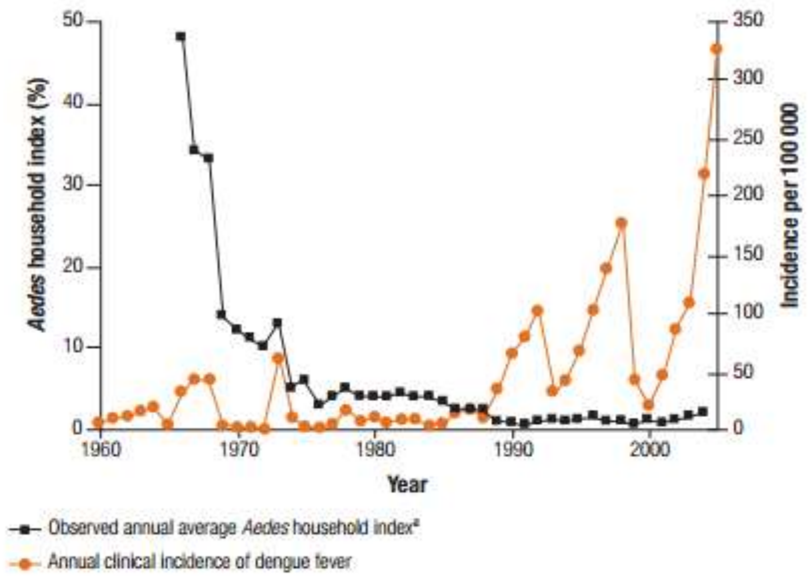
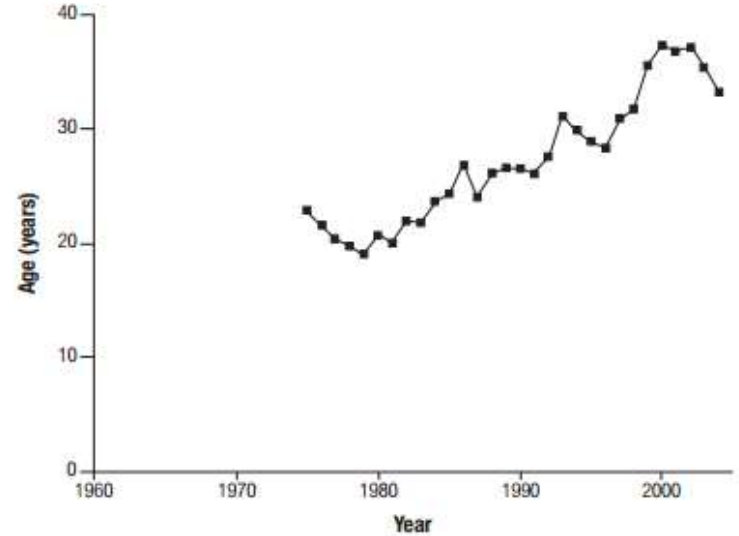
Discussion

Fig. 1. **Observed annual average *Aedes* household index and annual clinical incidence of dengue fever**



[a] 2005 household index estimate is not yet available.

Fig. 2. **Observed average age of clinical cases of dengue fever reported in Singapore[a]**



[a] National dengue control activities were instigated in 1966.

- Reduction in vectors, but increase in cases?
- Improved surveillance (majority non-severe cases)
- Decreased Immunity and increase in average age of clinical cases
- Possible need for genetically modified/Wolbacia infected mosquitoes or vaccine for elimination

Source: Egger et al. 2008

CONSISTENT EFFICACY PROFILE OF CYD 14 & CYD 15 IN SUBJECTS 9–16 YEARS OF AGE DURING ACTIVE PHASE

Key Efficacy Results

25-month active phase* Pooled efficacy analyses[‡1]

Reduction in symptomatic dengue

65.6%
(95% CI: 60.7–69.9)

For each serotype:

- DENV-1: 58.4% (95% CI: 47.7–66.9)
- DENV-2: 47.1% (95% CI: 31.3–59.2)
- DENV-3: 73.6% (95% CI: 64.4–80.4)
- DENV-4: 83.2% (95% CI: 76.2–88.2)

By dengue serostatus:

- Seropositive: 81.9% (95% CI: 67.2–90.0)
- Seronegative: 52.5% (95% CI: 5.9–76.1)

Reduction in hospitalized dengue

80.8%
(95% CI: 70.1–87.7)

Reduction in severe dengue[†]

92.9%
(95% CI: 76.1–97.9)

***Data come from the 2 pivotal, phase III, large-scale efficacy trials CYD14 and CYD15, which were designed to fully assess efficacy; postdose 1; [1]*Full Analysis Set for Efficacy (FASE): all* subjects who received at least one injection. [†]dengue hemorrhagic fever, World Health Organization 1997 criteria. CI=confidence interval; DENV=dengue virus.**

1.Hadinegoro, 2015, N Engl J Med.

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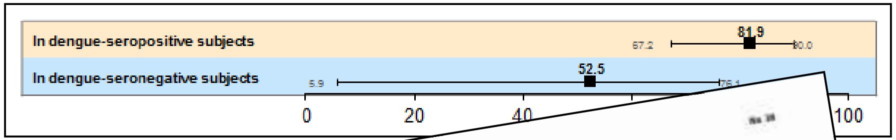
1.Hadinegoro, 2015, N Engl J Med.

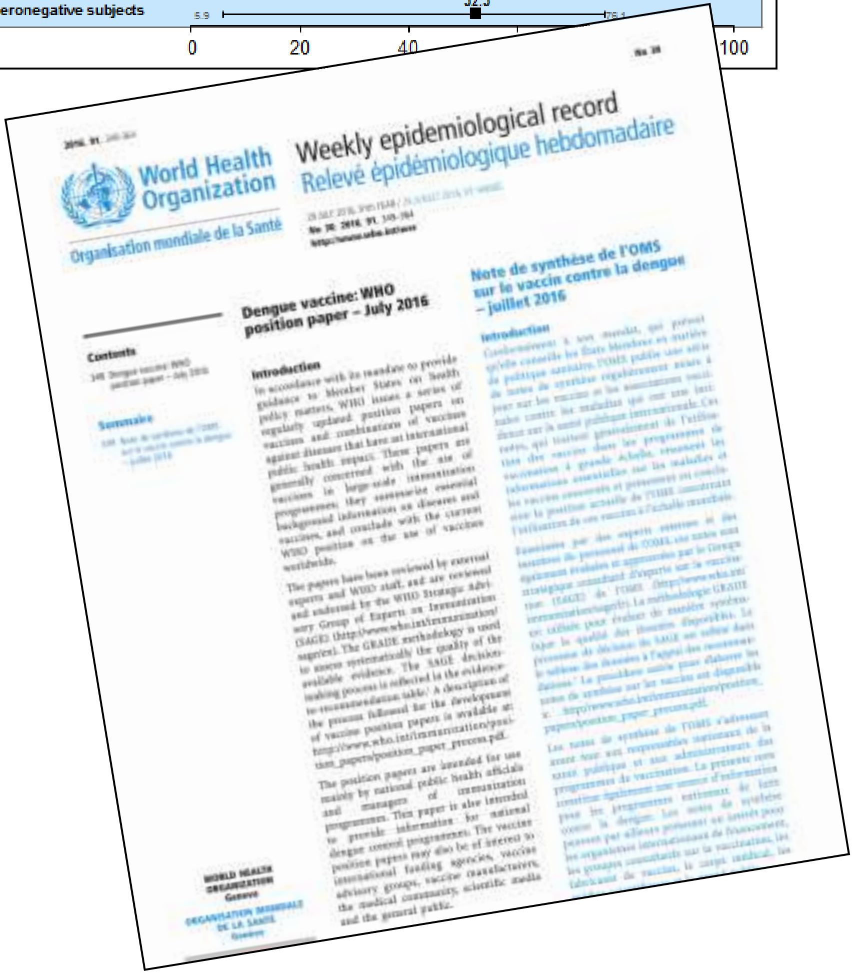
Clinical trials identified serostatus-specific efficacy. WHO recommends vaccine use in areas of high endemicity



“Prior infection, as measured by seroprevalence, should be approximately 70% or greater… to maximize public health impact and cost- effectiveness”

“Vaccination of populations with seroprevalence between 50% and 70% is acceptable”

“The vaccine is not recommended when seroprevalence is below 50% in the age group targeted for vaccination”



World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record

Relevé épidémiologique hebdomadaire

Dengue vaccine: WHO position paper – July 2016

Note de synthèse de l'OMS sur le vaccin contre la dengue – juillet 2016

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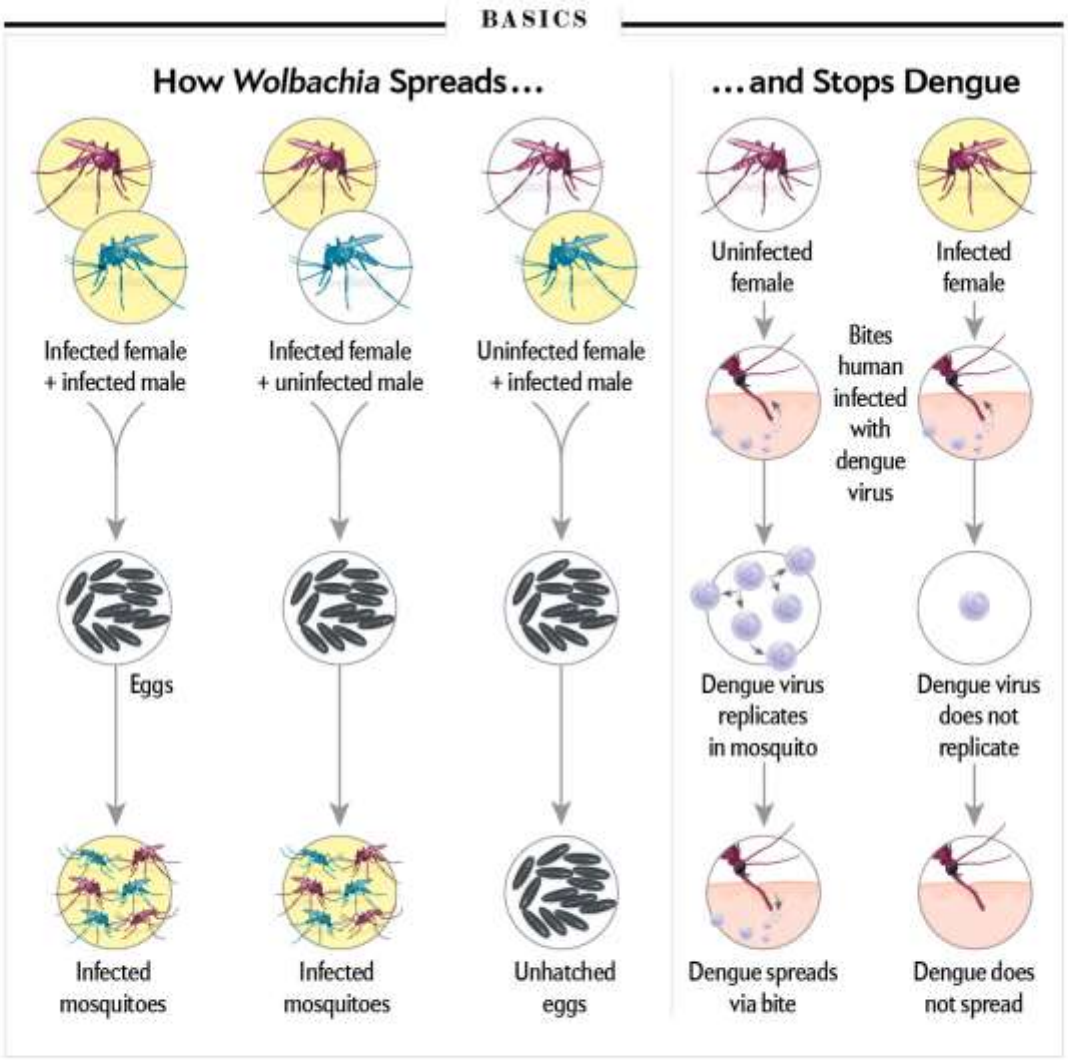
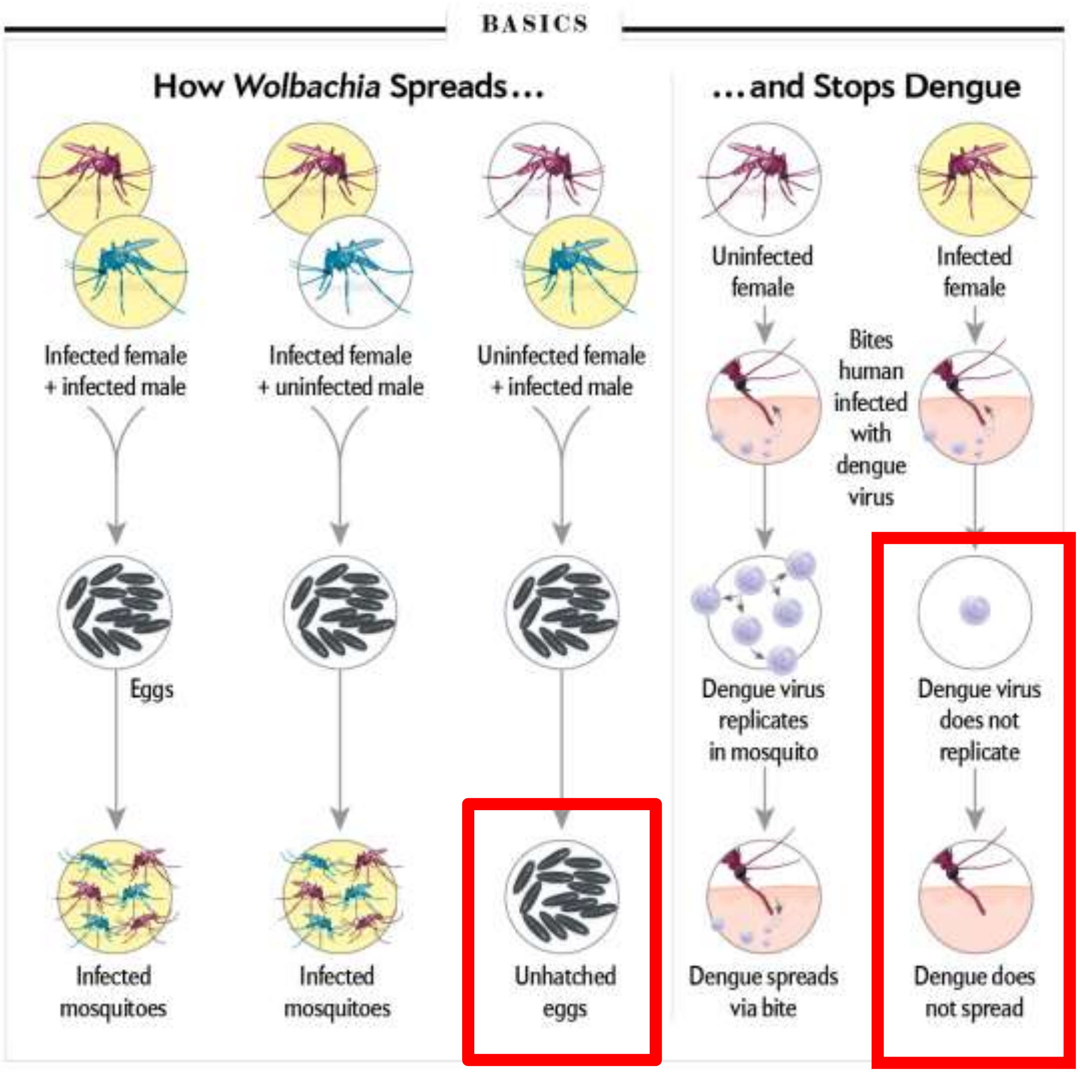
World Health Organization; Weekly epidemiological record 29 July 2016. 2016.

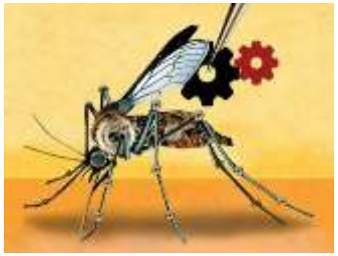
Wolbachia Infected Mosquitoes

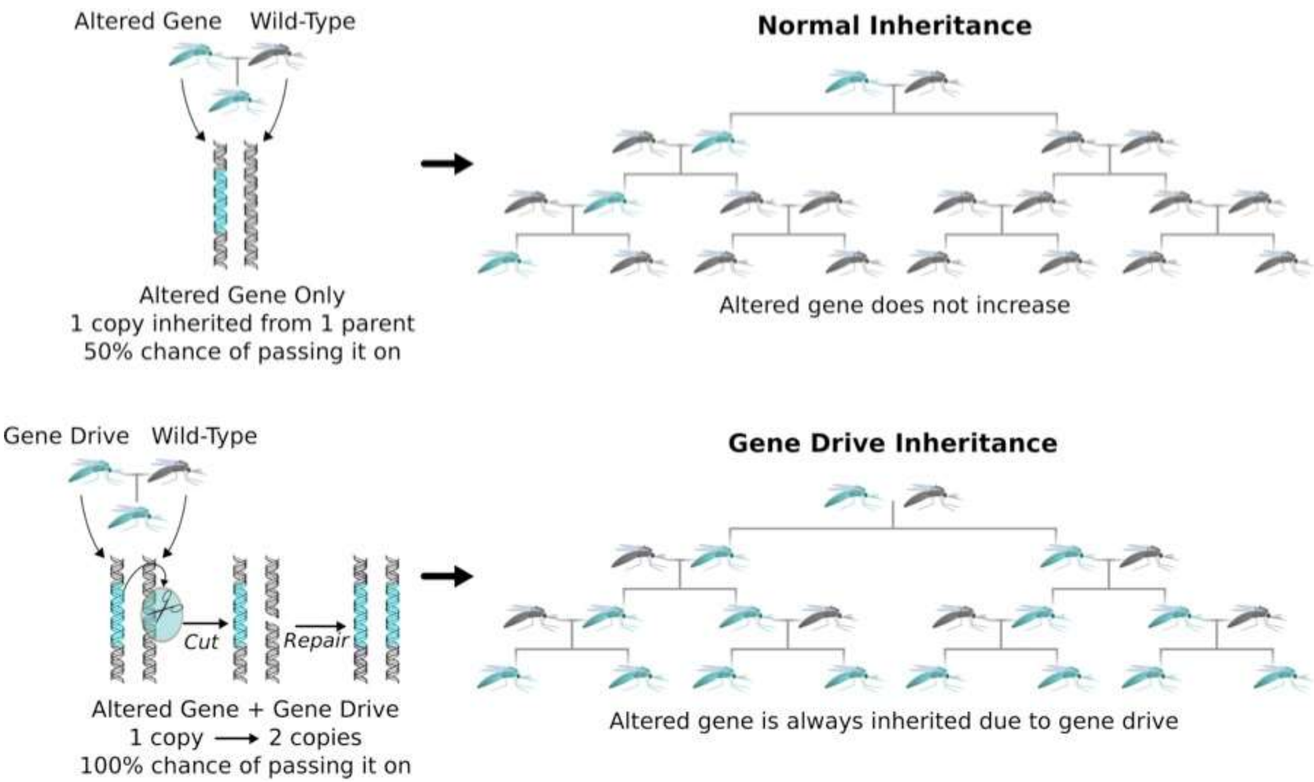


Wolbachia Infected Mosquitoes



Genetically modified mosquitoes





Source: Scientific American, 2014

Discussion

Waiting for perfect interventions such as new vaccines or genetically modified/wolbachia infected mosquitoes and abandoning traditional vector control tools is not best practice. Even with the introduction of new methods traditional tools can provide value:

- Effective environmental sanitation encouraged in COMBI activities can reduce incidence of enteric diseases, vector borne diseases and create healthier environments.
- Effective larval control can reduce mosquito populations impacting vector borne diseases for which we don't yet have effective vaccines (e.g. Zika, chikungunya) or are not targeted by modified mosquitoes.
- Community engagement strategies can help encourage uptake of any additional measures that may come in the future

Thank you

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