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# Long Lasting Insecticidal Treated Nets for malaria control: Success and challenges!

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# BACKGROUND



- A Long Lasting Insecticidal Nets (LN) is a factory-treated mosquito net expected to retain its biological activity for a minimum 20 standard washes and a minimum of 3 years under field conditions (WHO 2006).
- Actual WHO position on the use of LNs for malaria prevention is achieving full coverage by distributing LNs through existing public health services (WHO 2007)
- LN showed to be highly cost effective compared to ITN (2 times cheaper) and IRS (4–5 times cheaper) especially in malaria endemic area (Yukish et al. 2007)
- About 250 millions ITN (mainly LLIN) were distributed between 2004-2008 and such strategy showed strong reduction of malaria morbidity and mortality in different settings of transmission (Lengeler 2004, WHO 2007, 2009)



# ITN use and malaria morbidity

Country	EIR	Morbidity Reduction	Authors
Gambia	1-10 (S)	- 45%	Snow et al., 1987
Gambia	1 – 10 (S)	- 63%	Snow et al., 1988
Kenya	300 (P)	- 30%	Sexton et al., 1990
Kenya	300 (P)	- 40%	Beach et al., 1993
Gambie	1 – 10	- 45%	Alonso et al., 1993
Guinea Bissau	20-50 (S)	- 29%	Jaenson et al. 1994
Sierra Leone	20 – 40 (S)	- 49%	Marbiah 1995
Tanzania	300 (P)	- 55%	Premij et al., 1995
Kenya	10-30 (S)	- 44%	Nevill et al., 1996



# ITN use and child mortality

Country	EIR	Coverage	Reduction Mortality	Authors
Gambia	1-10 (S)	High	- 63%	Alonso <i>et al.</i> , 1991
Gambia	1 – 10 (S)	Medium	- 25%	D'Alessandro <i>et al.</i> , 1995
Kenya	10 – 30 (S)	High	- 33%	Nevill <i>et al.</i> , 1996
Ghana	100 – 300 (S)	High	- 17%	Binka <i>et al.</i> , 1996

# WHOPES Evaluation & Testing of LNs

Phase	Type of study	Activities
Phase I	Laboratory	<ul style="list-style-type: none"> <li>• Regeneration of insecticide and wash resistance</li> <li>• Efficacy</li> </ul>
Phase II	Small-scale field trials	<ul style="list-style-type: none"> <li>• Wash resistance</li> <li>• Efficacy and impact on vector behaviour</li> <li>• Safety observations</li> </ul>
Phase III	Large-scale field trials	<ul style="list-style-type: none"> <li>• Long-lasting efficacy</li> <li>• Community acceptance</li> <li>• Safety observations</li> </ul>

## Phase I



Cone bioassays



WHO wash



Tunnel tests

*If after 20 WHO washes*

> 80% mortality  
> 95% KD

> 80% mortality  
> 90% Blood feed. Inh.

**Meet the criteria to undergo Phase II testing**

## Phase II



West African Huts



Mosquito nets



East African huts

« If after 20 WHO washes, the LN performed equal or better than a conventionally treated net washed until just before exhaustion »

**Meet the criteria to undergo Phase III testing**  
(Interim recommendation)

## Phase III



Net Observation



Net collection



Bioassays

“If, at the end of the 3 years, at least 80% of nets meet the cut-off criteria for cone bioassays and/or tunnel test”

**The product meets the definition for an LN**  
(Full recommendation)

# WHO recommended LNs and Treatments

- Long-lasting insecticidal mosquito nets

Updated September 2010

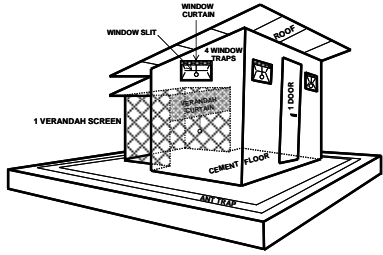
<i>Product name</i>	<i>Product type</i>	<i>Status of WHO recommendation</i>	<i>Status of publication of WHO specification</i>
<i>DawaPlus<sup>®</sup> 2.0</i>	Deltamethrin coated on polyester	Interim	Published
<i>Durane<sup>®</sup></i>	Alpha-cypermethrin incorporated into polyethylene	Interim	Published
<i>Interceptor<sup>®</sup></i>	Alpha-cypermethrin coated on polyester	Interim	Published
<i>Netprotect<sup>®</sup></i>	Deltamethrin incorporated into polyethylene	Interim	Published
<i>Olyset<sup>®</sup></i>	Permethrin incorporated into polyethylene	Full	Published
<i>PermaNet<sup>®</sup> 2.0</i>	Deltamethrin coated on polyester	Full	Published
<i>PermaNet<sup>®</sup> 2.5</i>	Deltamethrin coated on polyester with strengthened border	Interim	Published
<i>PermaNet<sup>®</sup> 3.0</i>	Combination of deltamethrin coated on polyester with strengthened border (side panels) and deltamethrin and PBO incorporated into polyethylene (roof)	Interim	Under development
<i>Yorkool<sup>®</sup> LN</i>	Deltamethrin coated on polyester	Full	Published

- Long-lasting treatments

Updated December 2007

<i>Product name</i>	<i>Product type</i>	<i>Status of WHO recommendation</i>
<i>ICON<sup>®</sup> MAXX</i>	Lambda-cyhalothrin 10% CS + binder Target dose of 50 mg/m <sup>2</sup>	Interim

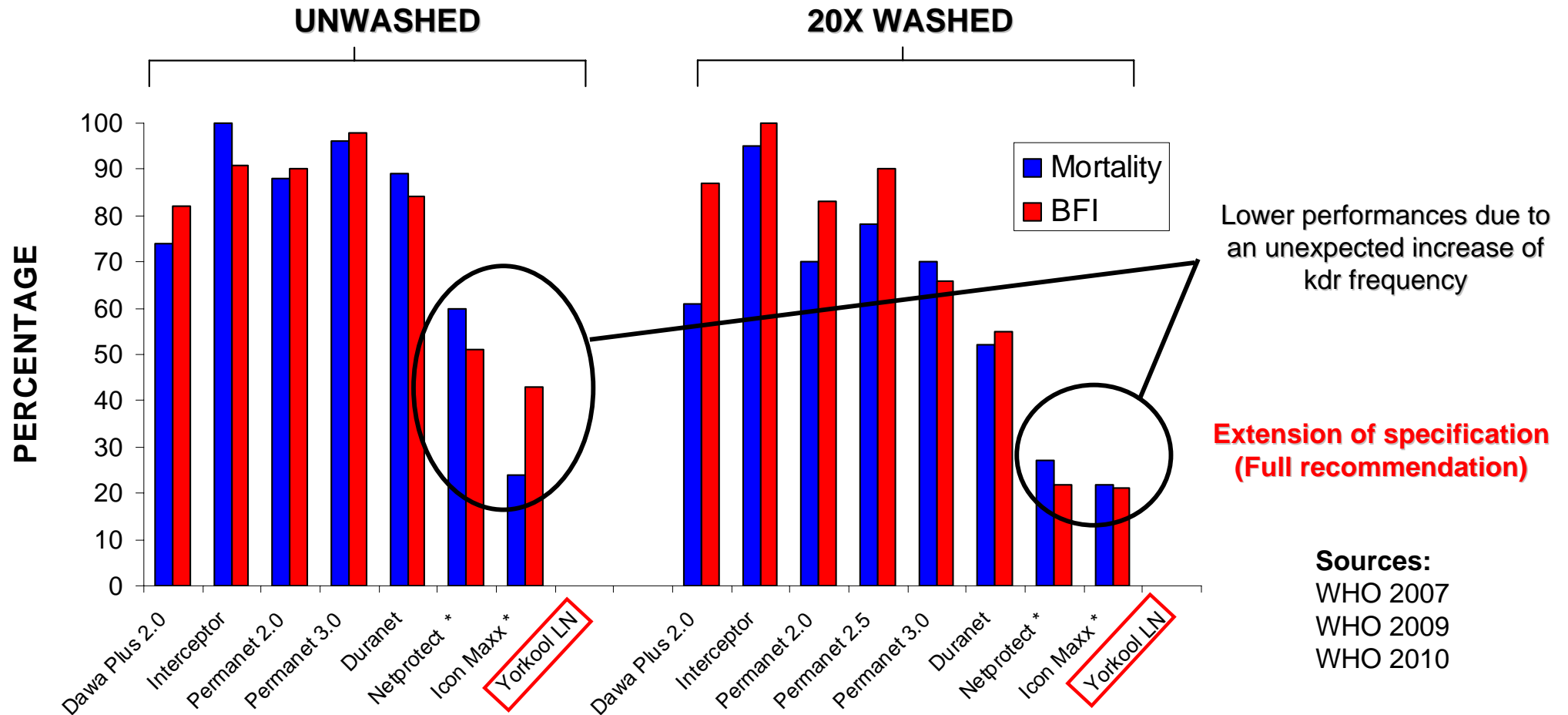




# Comparative performances of LNs in Phase II



WHOPES supervised huts trials in West Africa (Susceptible area)

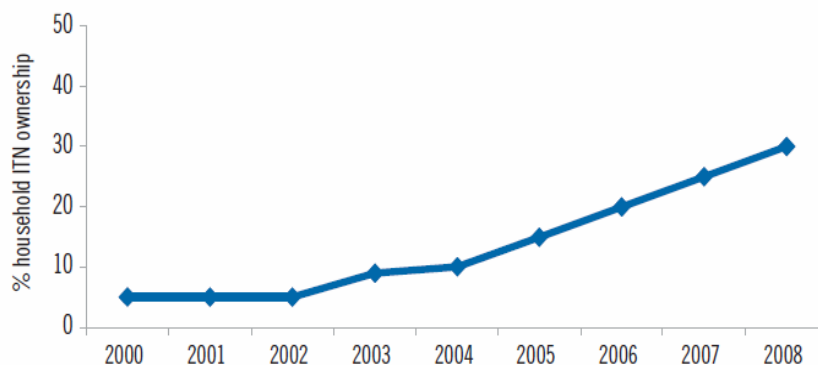


# Limitations of LNs for malaria control

- Acceptability by populations
- Coverage / use
- LN replacement (avoid misuse)
- Absence of impact on early/outdoor biters mosquitoes
- Spread of pyrethroid resistance in malaria vectors



Figure 3.11 Percentage household ownership of insecticide-treated nets (ITNs) estimated from model, 2000–2008, 35 high-burden WHO African Region countries



« The WHO malaria report 2009 estimates that 31% of African households owned at least one ITN, and 24% of children under 5 years of age had used an ITN in 2008 »



# Pyrethroid Resistance & ITN efficacy

**Malaria Journal**



Research

Open Access

**Dosage-dependent effects of permethrin-treated nets on the behaviour of *Anopheles gambiae* and the selection of pyrethroid resistance**

Vincent Corbel<sup>\*1</sup>, Fabrice Chandre<sup>2</sup>, Cécile Brengues<sup>1</sup>, Martin Akogbeto<sup>2</sup>, Frédéric Lardeux<sup>3</sup>, Jean Marc Hougard<sup>2</sup> and Pierre Guillet<sup>4</sup>

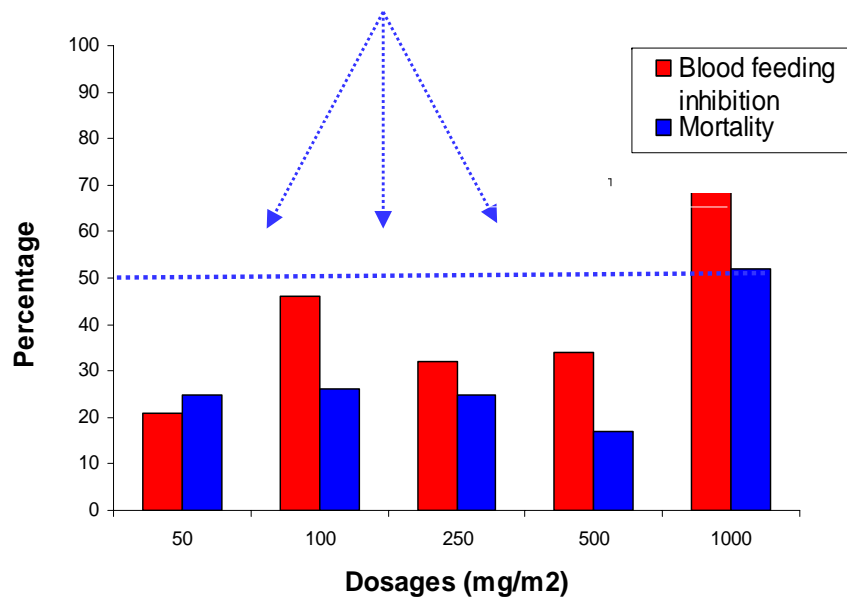


Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 2, February 2007

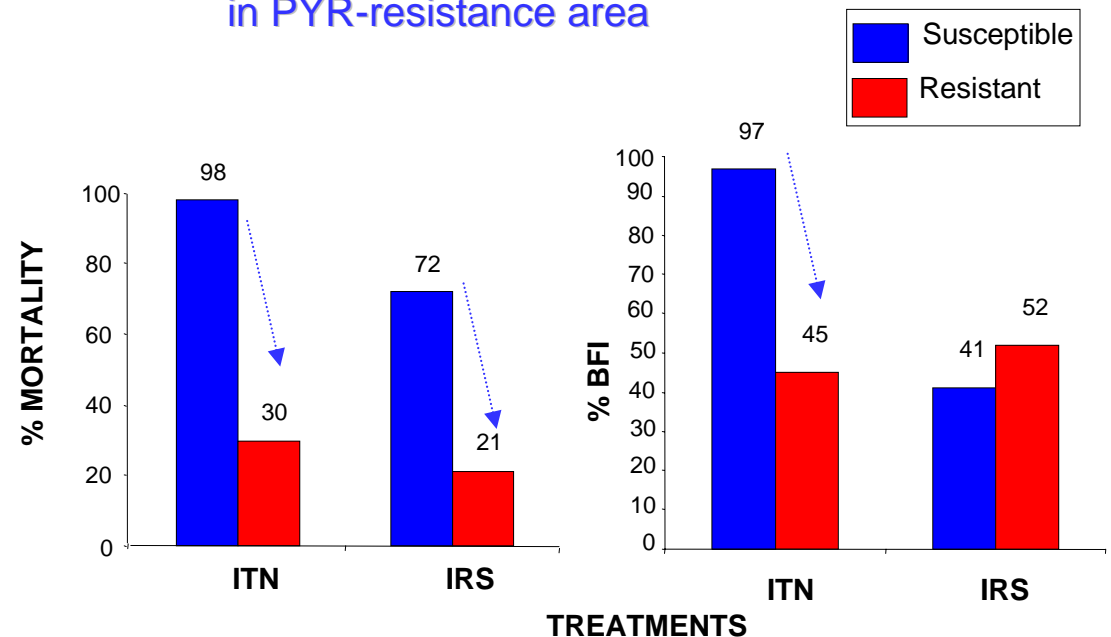
## Reduced Efficacy of Insecticide-treated Nets and Indoor Residual Spraying for Malaria Control in Pyrethroid Resistance Area, Benin

Raphael N'Guessan,<sup>\*</sup> Vincent Corbel,<sup>†</sup> Martin Akogbeto,<sup>‡§</sup> and Mark Rowland<sup>¶</sup>

Low blood feeding inhibition with Permethrin Treated Nets against *kdr*-resistant *An. gambiae*

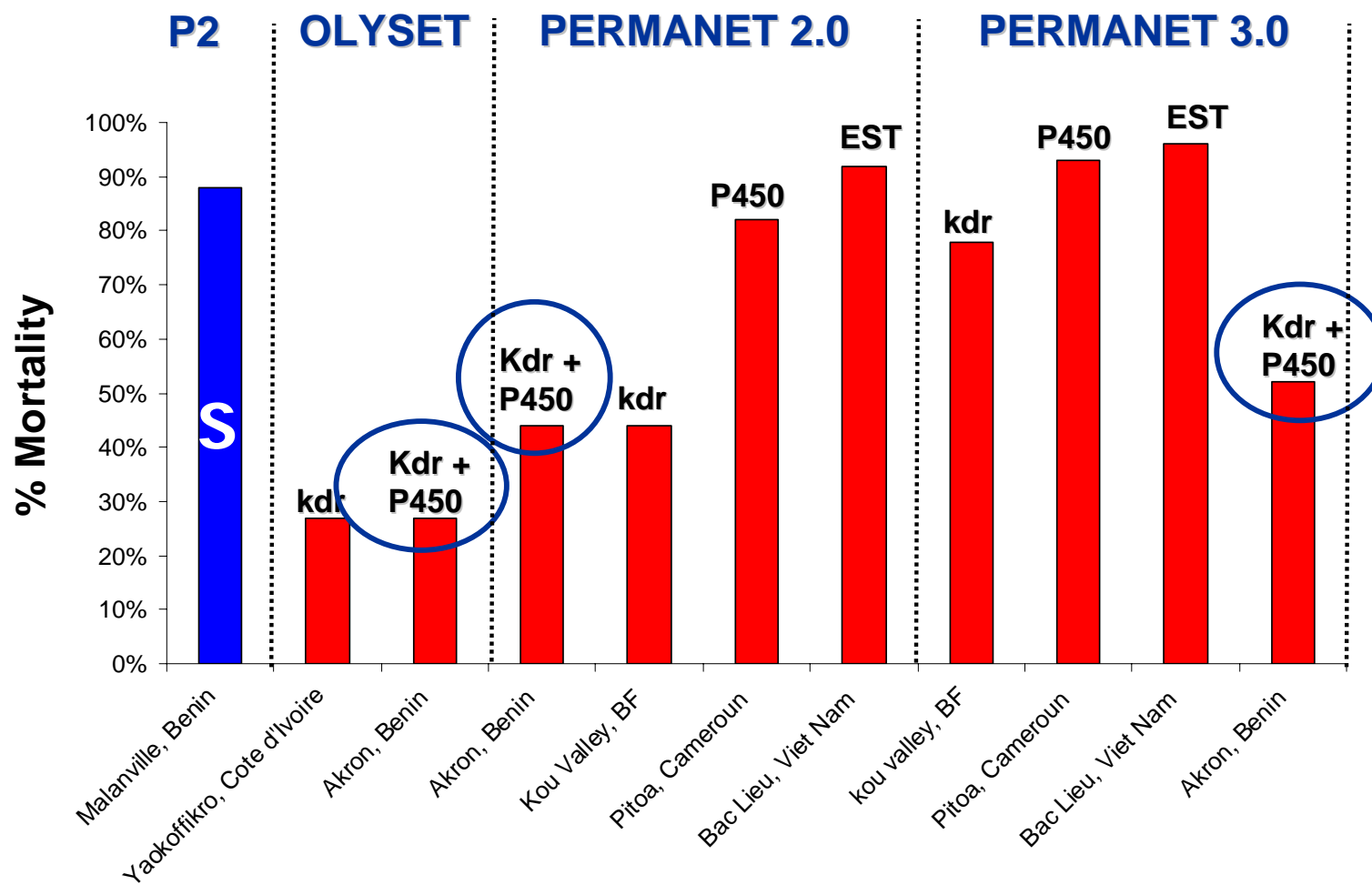


Loss of efficacy of ITN and IRS in PYR-resistance area



# Pyrethroid Resistance & LN efficacy

Insecticidal activity of several WHO recommended LNs against **pyrethroid-resistant** malaria vectors



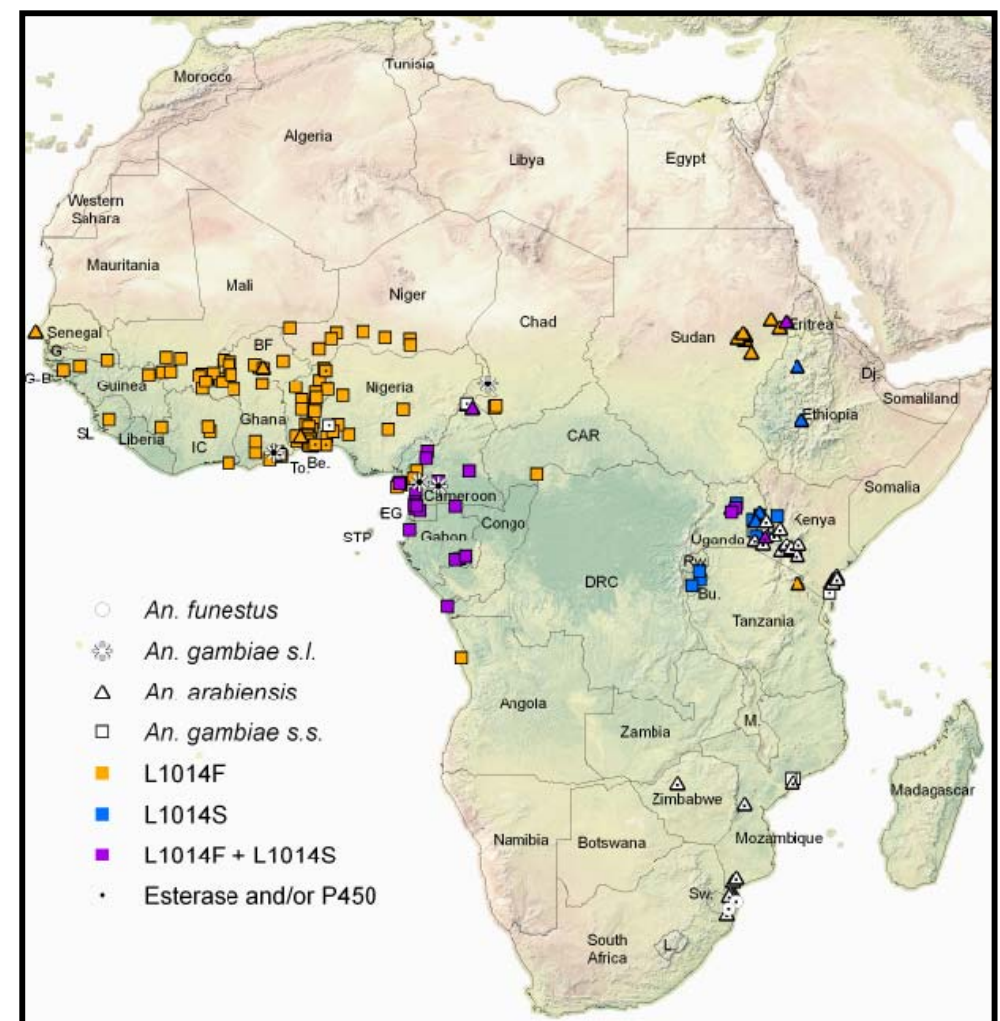
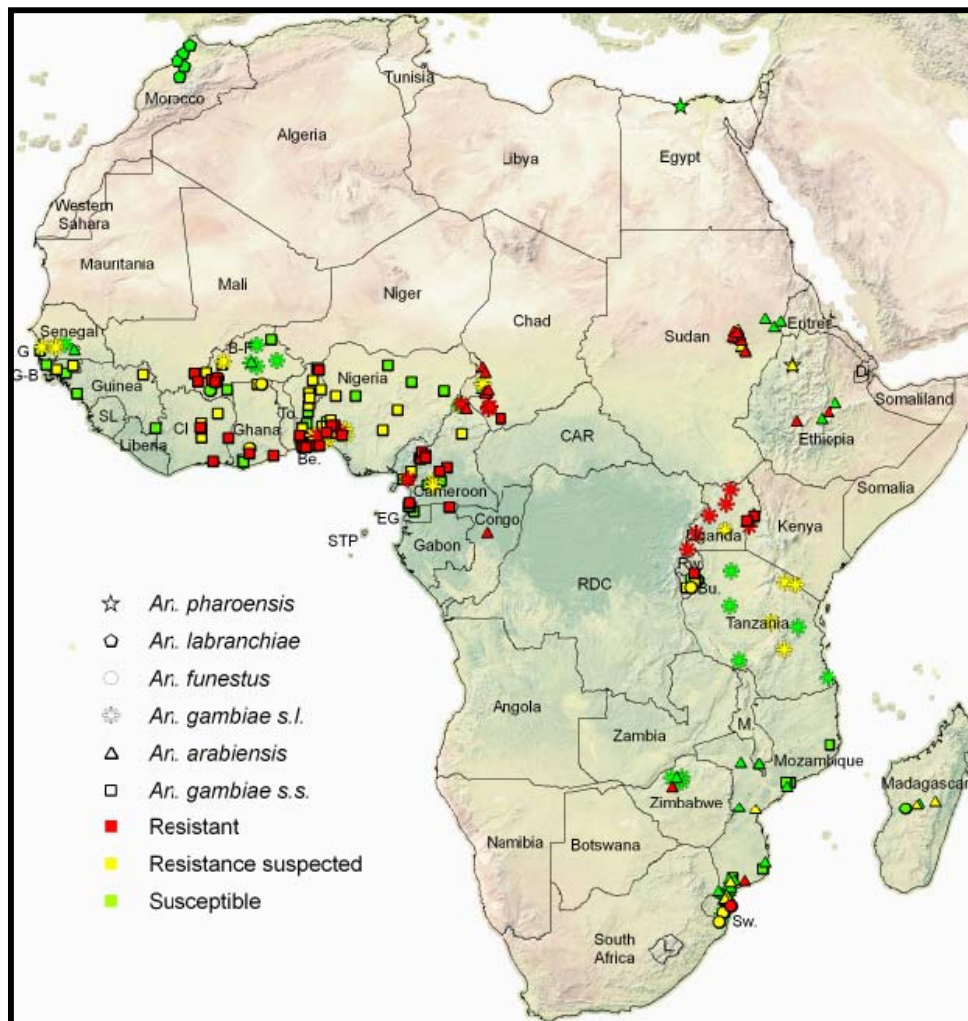
Strong impact  
of multiple  
resistance on  
LN efficacy

## Sources:

WHO 2009  
Corbel et al 2010  
N'Guessan et al 2001  
N'Guessan et al 2010  
Van Bortel et al 2009

# Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control?

Hilary Ranson<sup>1</sup>, Raphael N'Guessan<sup>2,5</sup>, Jonathan Lines<sup>3</sup>, Nicolas Moiroux<sup>4,5</sup>, Zinga Nkuni<sup>3</sup> and Vincent Corbel<sup>4,5</sup>





# Combination of LLIN and IRS for malaria vector control ?

**Malaria Journal**

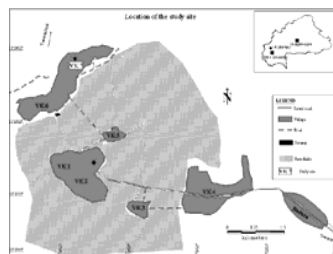


Research

Open Access

**Managing insecticide resistance in malaria vectors by combining carbamate-treated plastic wall sheeting and pyrethroid-treated bed nets**

Armel Djènontin<sup>1,2</sup>, Joseph Chabi<sup>2</sup>, Thierry Baldet<sup>2</sup>, Seth Irish<sup>4</sup>, Cédric Pennetier<sup>3</sup>, Jean-Marc Hougard<sup>2</sup>, Vincent Corbel<sup>\*2</sup>, Martin Akogbéto<sup>1</sup> and Fabrice Chandre<sup>3</sup>

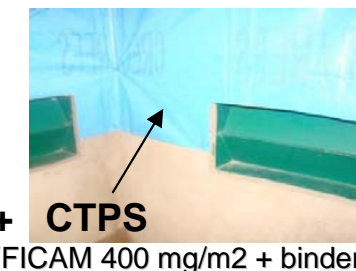
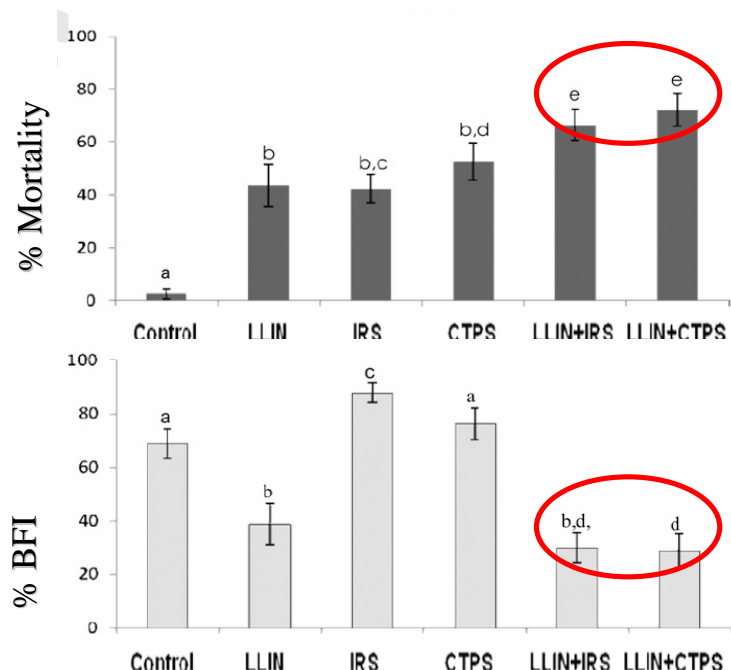


*Am. J. Trop. Med. Hyg.*, 83(2), 2010, pp. 266–270  
doi:10.4269/ajtmh.2010.10-0012  
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Indoor Use of Plastic Sheetting Impregnated with Carbamate Combined with Long-Lasting Insecticidal Mosquito Nets for the Control of Pyrethroid-Resistant Malaria Vectors

Armel Djènontin,\* Fabrice Chandre, K. Roch Dabiré, Joseph Chabi, Raphael N'Guessan, Thierry Baldet, Martin Akogbéto, and Vincent Corbel

## Experimental huts trial in Burkina Faso



- Increase mortality and reduced blood feeding rates by combining LLIN and IRS (or CTPS)
- No selection for the *kdr* and *Ace. 1* resistant alleles
- Possibility to develop Long Lasting Technology for Plastic Sheetting on walls (ITPS, DL)
- RCT trial ongoing in Southern Benin to demonstrate their efficacy for reducing malaria transmission & morbidity



# CONCLUSION



- Pyrethroid resistance in malaria vectors is a growing problem that may seriously threaten the malaria related MDG (75% reduction of malaria burden by 2015)
- More public health evidence on the impact of IR on Vector Control required (including combined strategy) through robust epidemiological studies (e.g. RCT)
- Better knowledge on the genetic basis of IR needed to develop reliable diagnostic test for regular monitoring of metabolic resistance and set up “EARLY” IRM strategies in the field.
- More investment on R&D required to provide PH sector with new A.I classes for LN (and IRS) (extending collaboration with Gates Foundation, Industries, WHOPEs, etc.)

*Thanks for your attention....*

