



Insecticide resistance in West Africa





...to develop new tools and knowledge that will complement existing strategies to ensure the continued success of malaria vector control in the era of insecticide resistance.....



University of
Crete



CSRS
Centre Suisse de Recherches
Scientifiques en Côte d'Ivoire





- Growing cross resistance across insecticide classes: lessons from Tiassalé
- When diagnostic dose bioassays are not enough: comparing approaches to measure strength and impact of resistance



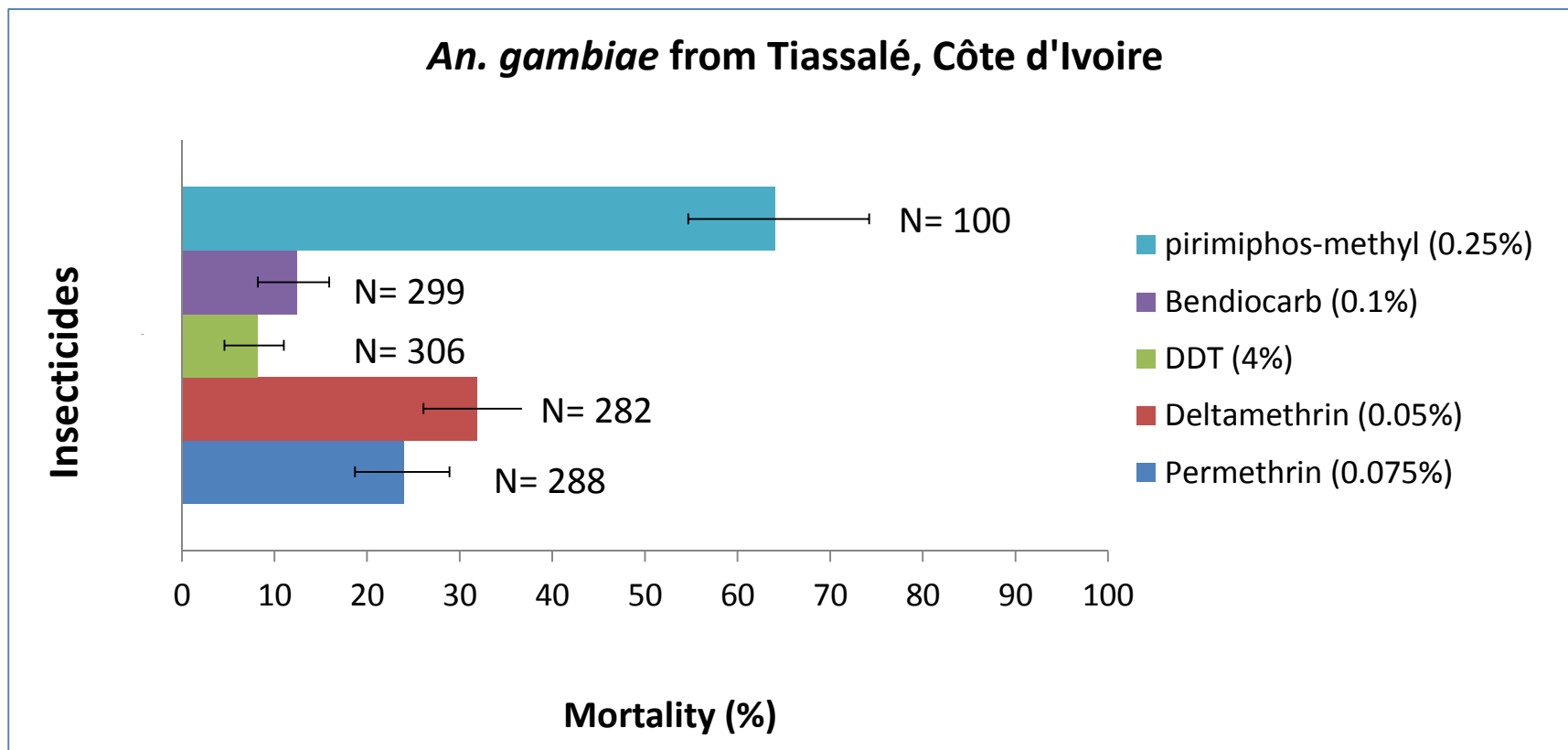
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The Tiassalé population of *Anopheles gambiae* from Côte d'Ivoire is resistant to all classes of insecticides available for IRS (results of WHO diagnostic dose assays)



Resistance Ratios (estimated by LT50) to pyrethroids > 24 x carbamates, 68 x type I pyrethroids, 330 x type II pyrethroids

3 minute exposure to LLIN does not kill this strain.

The Tiassalé stain: A potent mix of resistance mechanisms

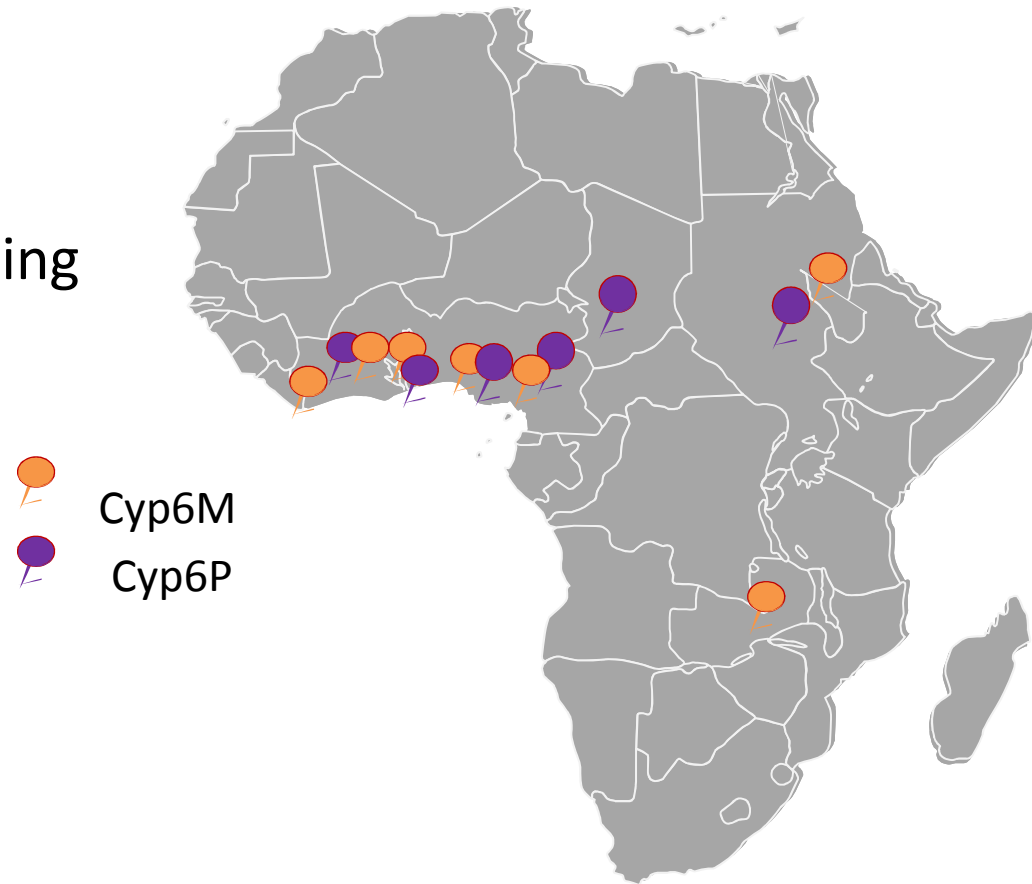
- Very high frequency of the target site mutation, kdr (1014F kdr allele > 0.8)
- Very high frequency of insensitive acetylcholinesterase (> 90 % of the population heterozygous for G119S)
- Gene duplication at the acetylcholinesterase locus (conferring additional resistance to bendiocarb)
- Elevated expression of CYP6M2 (increases rate of detoxification of pyrethroids, DDT and *primiphos-methyl*)
- Elevated expression of multiple CYP6P enzymes (increases rate of detoxification of pyrethroids and bendiocarb)

	P450	Deltamethrin	Permethrin	Lambdacyhalothrin	Bifenthrin	Cypermethrin	Etofenprox	DDT	Bendiocarb
CYP6P3	Mean % depletion	98.2	100.0	83.3	76.7	98.4	99.8	19.5	64.2
	SD	0.1	0.0	15.4	0.3	0.1	0.3	4.9	4.0
CYP6M2	Mean % depletion	55.4	58.5	49.4	38.9	36.4	68.8	41.6	0
	SD	1.4	2.2	0.5	1.6	1.82	1.1	0.16	11.2



All resistance mechanisms present in Tiassalé are also found elsewhere in Africa

- Kdr widespread
- Insensitive ace-1 spreading in West Africa

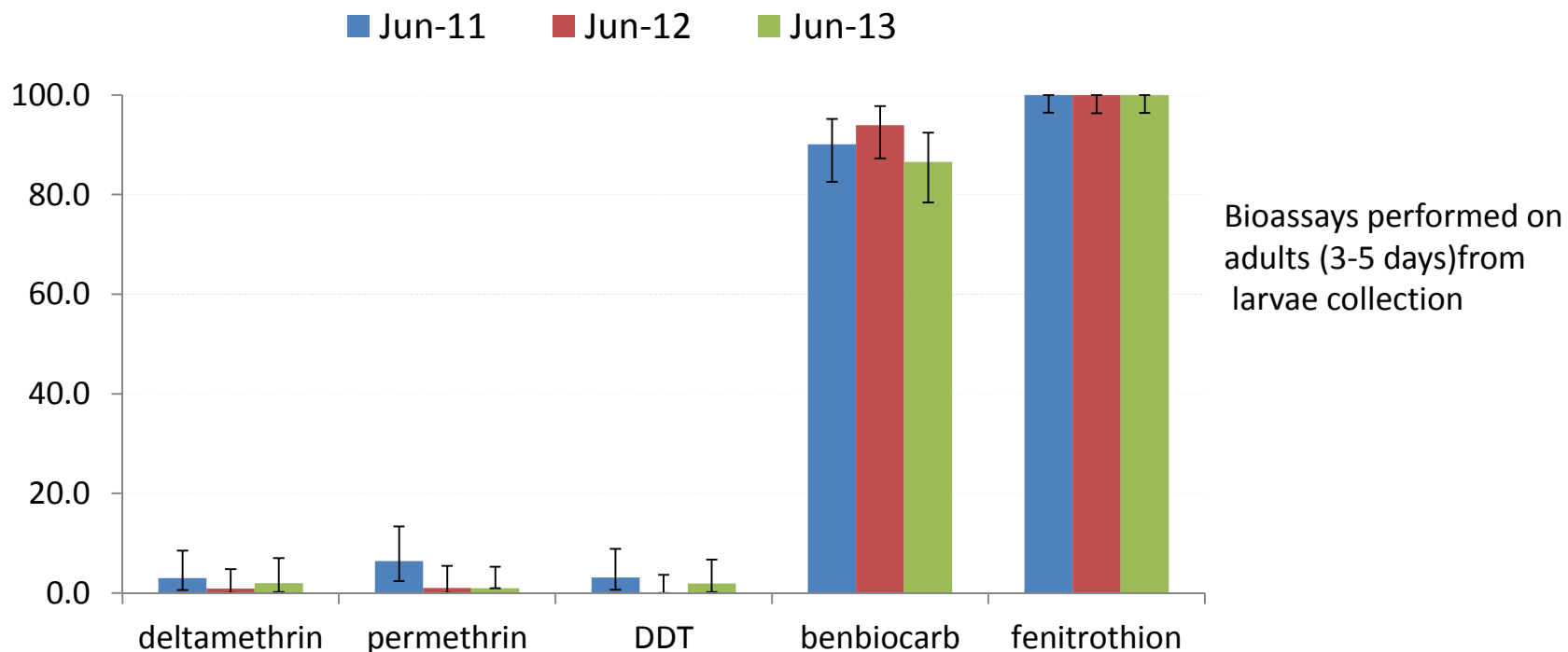


When diagnostic dose bioassays are not enough: comparing approaches to measure strength and impact of resistance

Pyrethroid resistance in Burkina Faso



Three years of WHO monitoring show very little change in resistance in Valle de Kou, Burkina Faso



When resistance is established in a population, diagnostic assays may mask drastic changes in the resistance levels – how do we measure this (and interpret the data)

How to quantify the level of resistance in the population?

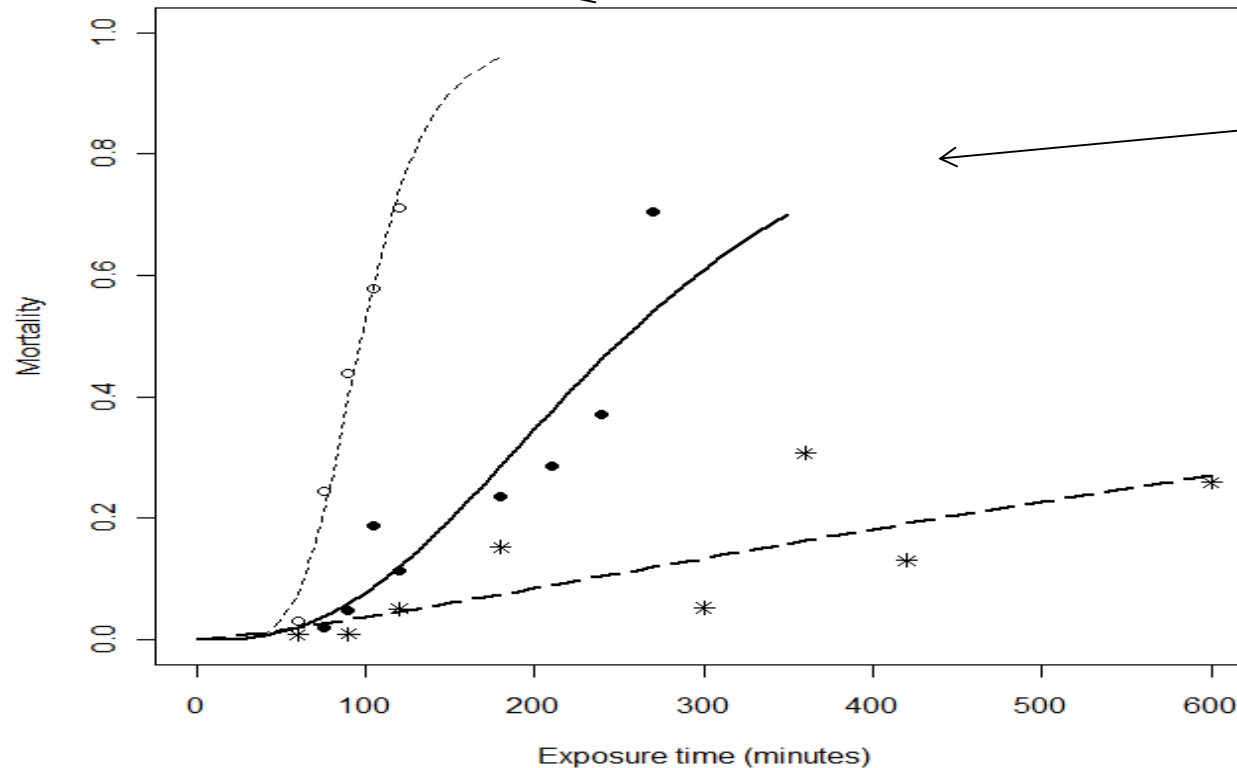
- WHO Diagnostic doses from 2010-2013
- WHO tube bioassays with varying time of exposure (LT50) from 2011-2012
- Cone bioassays on nets 2012
- CDC bottle bioassays (with 24 hour mortality recorded) with varying insecticide concentrations (LC50) 2013

- How do data vary between years/assay methods?
- Which method is most reliable and useful?
- What are the major sources of variability?



LT50 determination shows 10 x increase in resistance level
in single year (Exposure to 0.05 % Deltamethrin papers).

July 2011



October 2011

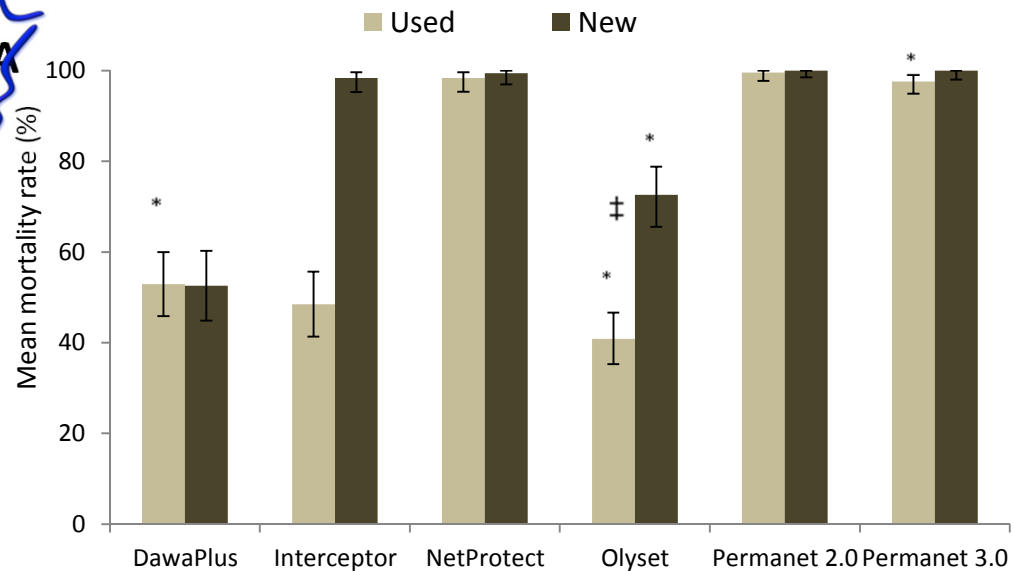
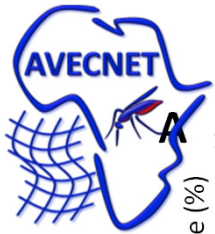
June 2012

July 2011: 97.80 min (93.90-101.90)

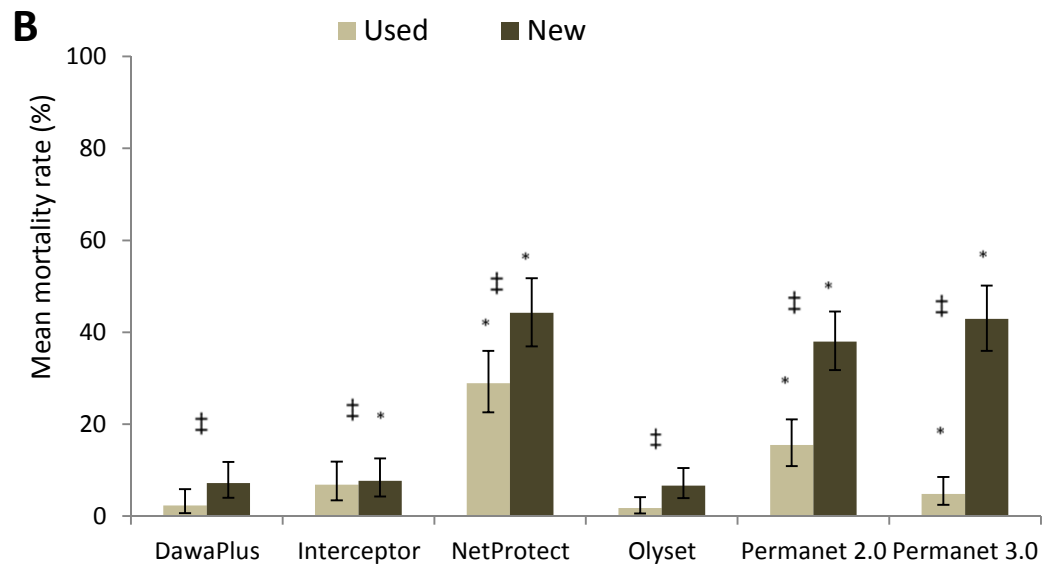
October 2011: 253.90 min (233.10-276.5)

June 2012: 1315.9 min (842.80-2054.5) (but extrapolation required to estimate this value) (RR vs Kisumu = 650 x)



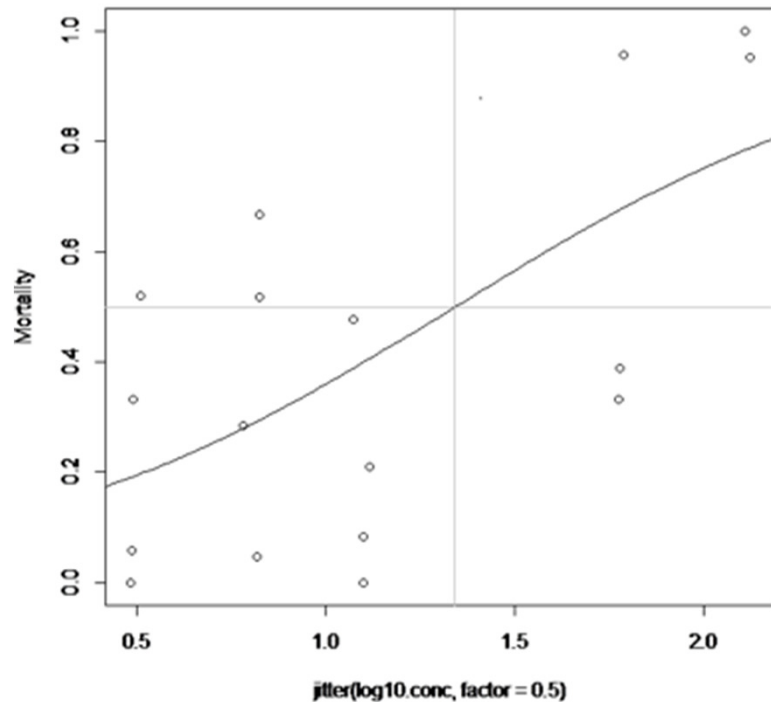


Mean mortality rate 24 hours after a 3' exposure to new and used different type of LLINs against Kisumu laboratory strain (A) and against the VK7 field strain (B)





CDC Bottle bioassays with deltamethrin (1 hour exposure, 24 hour recovery)



Data sets highly variable

Two 'estimate's obtained –

21.98 $\mu\text{g/ml}$ (CI: 15.74-30.68), July 2013

40.23 $\mu\text{g/ml}$ (CI: 34.11-47.44), Nov 2013

Kisumu lab strain 0.028 $\mu\text{g/ml}$ (CI: 0.021-0.038)

= RR of 785 – 1,436 X

What action to take when countries detect insecticide resistance?

- Are diagnostic dose assays alone sufficient to make recommendations on insecticide policy?
- If not, what else is needed?
 - Resistance ratio? (LT or LC?)
 - Cone bioassay data?
 - Molecular mechanisms?
- Can we define an 'operational significant level of resistance from a bioassay?
- Source of mosquitoes an important consideration
 - Resistance differs in adults raised from larval collections and F1 adults from wild caught females
 - Resistance can differ depending on time of year
 - etc

Linking bioassay and molecular data to resistance impact

