

Responding to pyrethroid resistance:

Sustaining malaria control using alternative insecticides

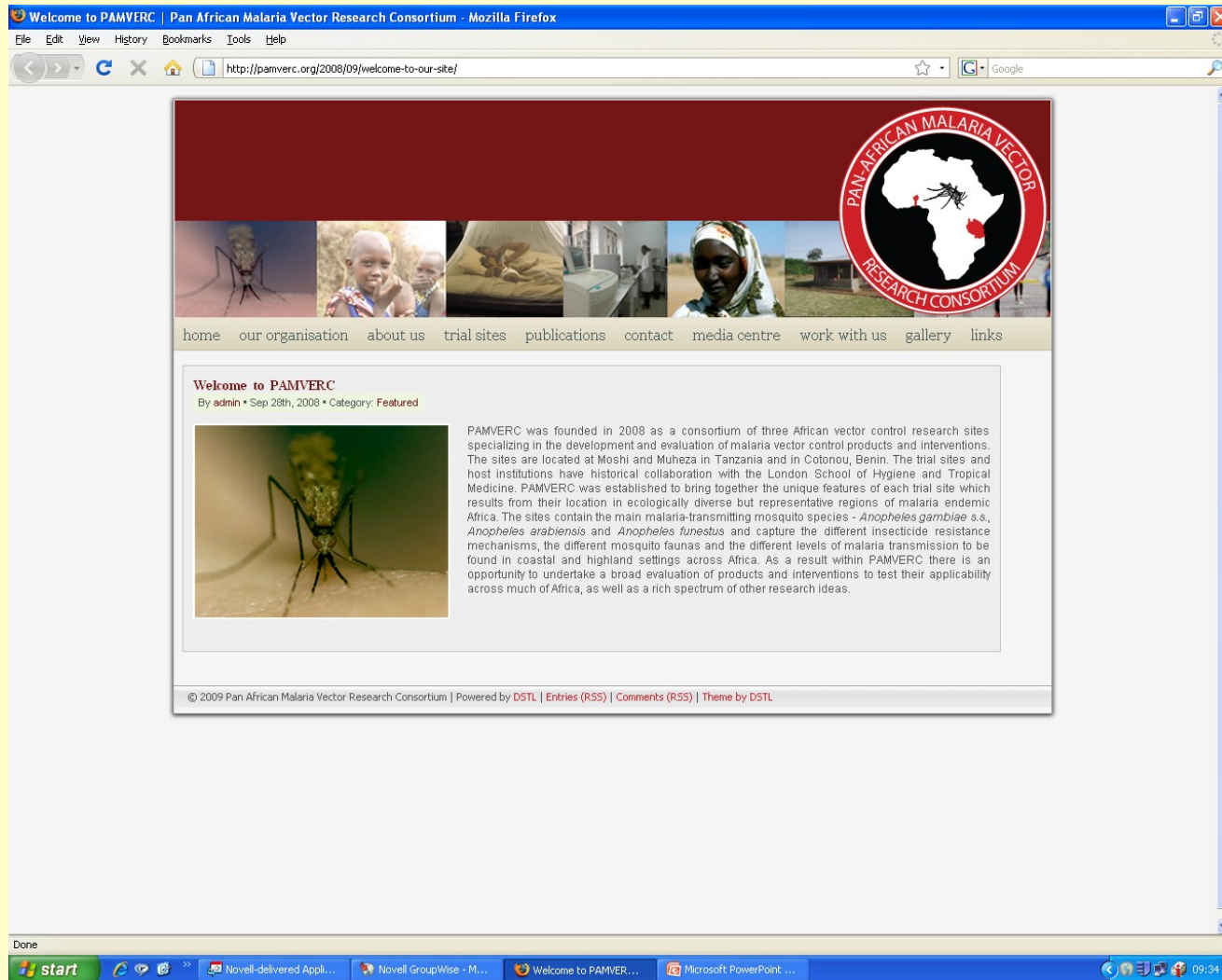
Mark Rowland



IVCC
COMBATING INSECT
BORNE DISEASE
The Innovative Vector
Control Consortium

PAMVERC trial site alliance

www.pamverc.org



The screenshot shows a Mozilla Firefox browser window displaying the PAMVERC website. The browser's address bar shows the URL <http://pamverc.org/2008/09/welcome-to-our-site/>. The website's header features a dark red banner with the PAMVERC logo on the right, which consists of a white map of Africa with a mosquito and a red flower, surrounded by the text "PAN-AFRICAN MALARIA VECTOR RESEARCH CONSORTIUM". Below the banner is a horizontal strip of six small images: a mosquito, two children, a person in a hospital bed, a person in a lab coat, a woman in a headscarf, and a building. A navigation menu below the images includes links for "home", "our organisation", "about us", "trial sites", "publications", "contact", "media centre", "work with us", "gallery", and "links". The main content area has a heading "Welcome to PAMVERC" by "admin" on "Sep 28th, 2008" in the "Featured" category. It includes a large image of a mosquito and a text block describing the consortium's mission and research sites. The footer of the website contains copyright information: "© 2009 Pan African Malaria Vector Research Consortium | Powered by DSTL | [Entries \(RSS\)](#) | [Comments \(RSS\)](#) | Theme by DSTL". The Windows taskbar at the bottom shows the Start button and several open applications, including "Novell-delivered Appli...", "Novell GroupWise - M...", "Welcome to PAMVER...", and "Microsoft PowerPoint...".

Welcome to PAMVERC | Pan African Malaria Vector Research Consortium - Mozilla Firefox


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Welcome to PAMVERC

By admin • Sep 28th, 2008 • Category: Featured



PAMVERC was founded in 2008 as a consortium of three African vector control research sites specializing in the development and evaluation of malaria vector control products and interventions. The sites are located at Moshi and Muheza in Tanzania and in Cotonou, Benin. The trial sites and host institutions have historical collaboration with the London School of Hygiene and Tropical Medicine. PAMVERC was established to bring together the unique features of each trial site which results from their location in ecologically diverse but representative regions of malaria endemic Africa. The sites contain the main malaria-transmitting mosquito species - *Anopheles gambiae* s.s., *Anopheles arabiensis* and *Anopheles funestus* and capture the different insecticide resistance mechanisms, the different mosquito faunas and the different levels of malaria transmission to be found in coastal and highland settings across Africa. As a result within PAMVERC there is an opportunity to undertake a broad evaluation of products and interventions to test their applicability across much of Africa, as well as a rich spectrum of other research ideas.

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Done

start Novell-delivered Appli... Novell GroupWise - M... Welcome to PAMVER... Microsoft PowerPoint...

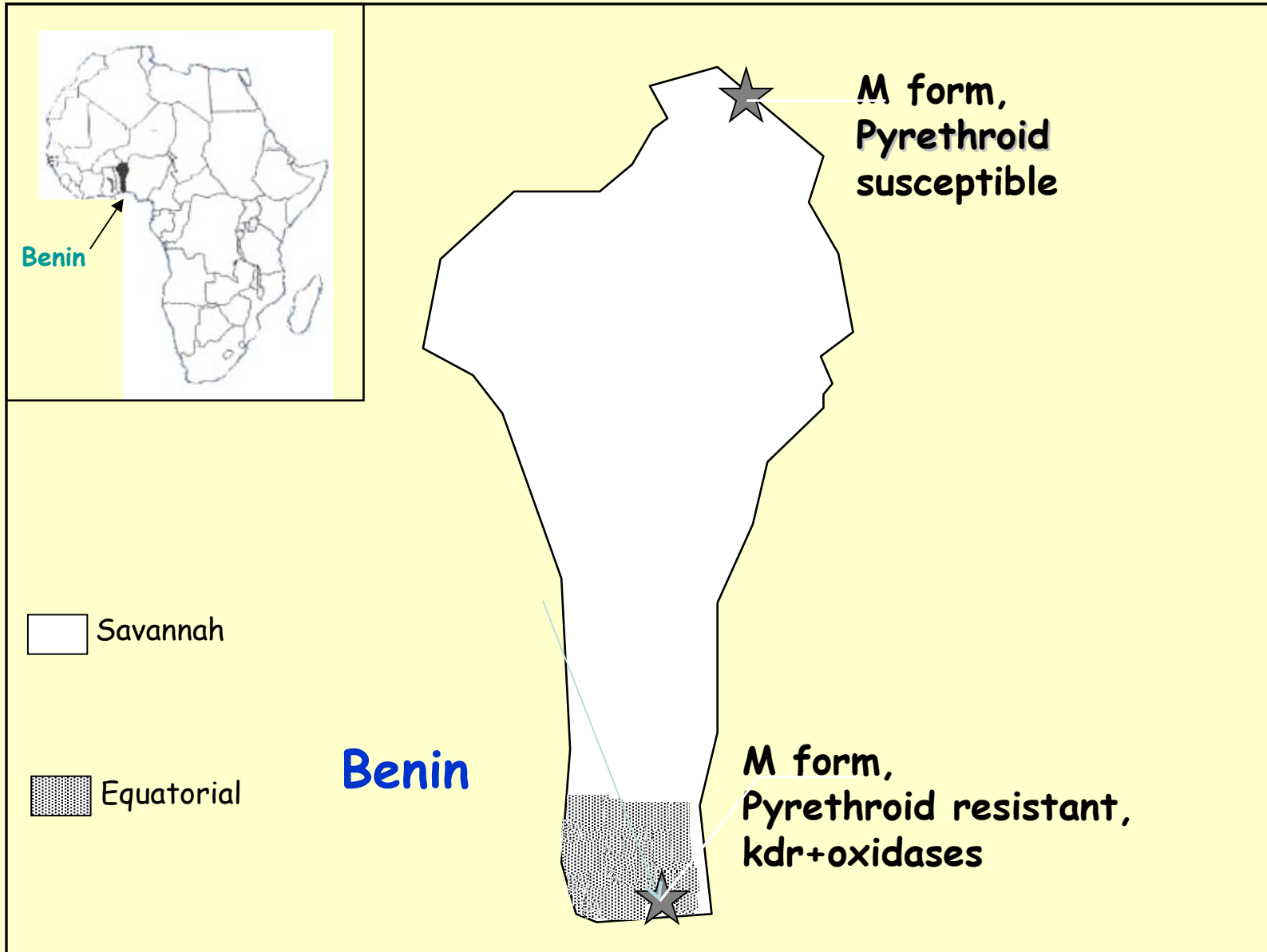
09:34

KCMC Moshi and NIMR Muheza in Tanzania, and CREC in Benin

Themes

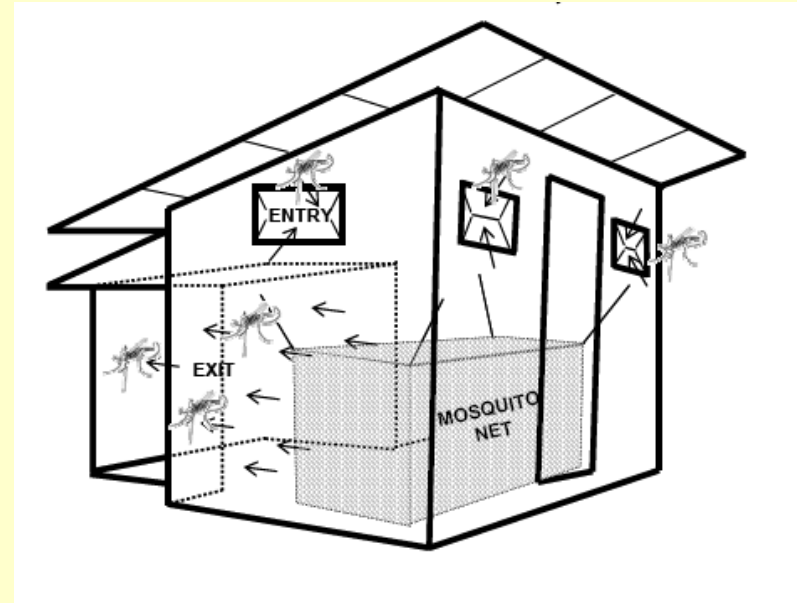
- Impact of pyrethroid resistance on ITNs and IRS
- Responding to resistance
 - Alternative insecticides on nets and IRS
 - Reformulation
 - Combinations

An. gambiae and resistance



- Does pyrethroid resistance reduce the effectiveness of ITN and IRS?
- Comparison of ITNs and IRS in areas of
 - pyrethroid resistance
 - pyrethroid susceptibility
- Experimental hut trials

What do experimental huts measure?



Insecticide performance under realistic, controlled conditions

Personal protection

Reduction in blood-feeding

Deterred mosquito entry

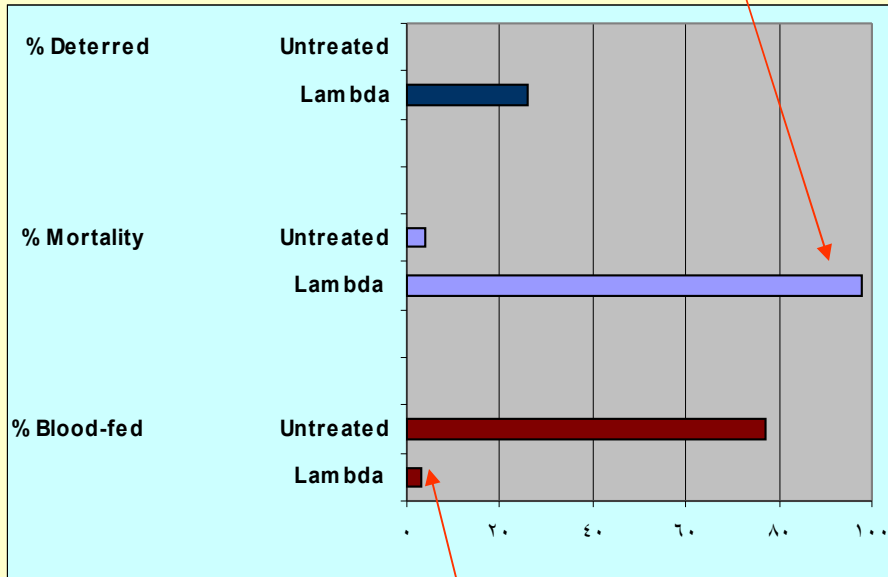
Transmission control potential

Mosquito mortality

Contrasting impact of pyrethroid ITN in N and S Benin (nets with 6 holes)

N Benin

Transmission control

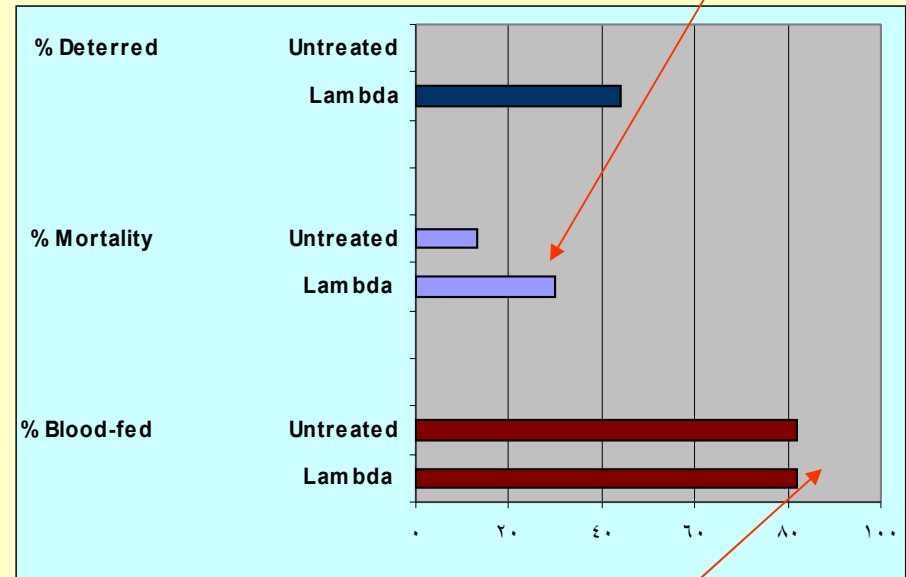


Personal protection

An gambiae M form (susceptible)

S. Benin

Transmission control lost?



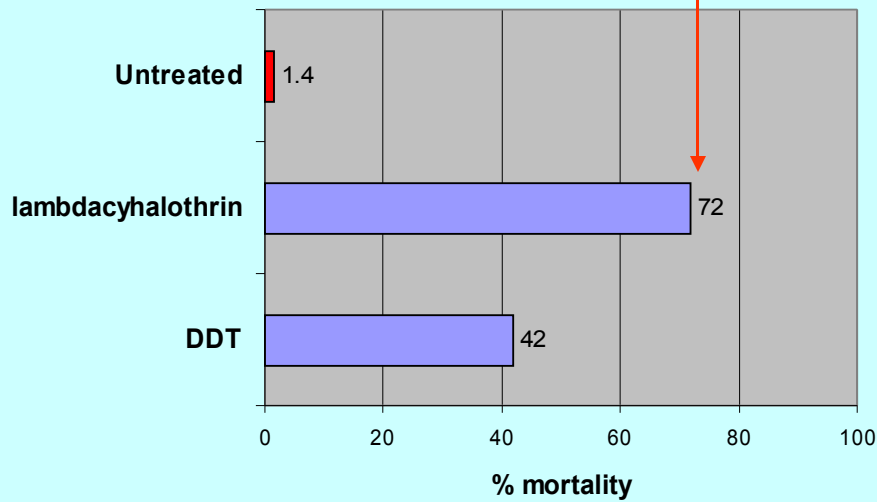
Personal protection lost

An gambiae M form (kdr+oxidases)

Contrasting impact of pyrethroid IRS in N and S Benin

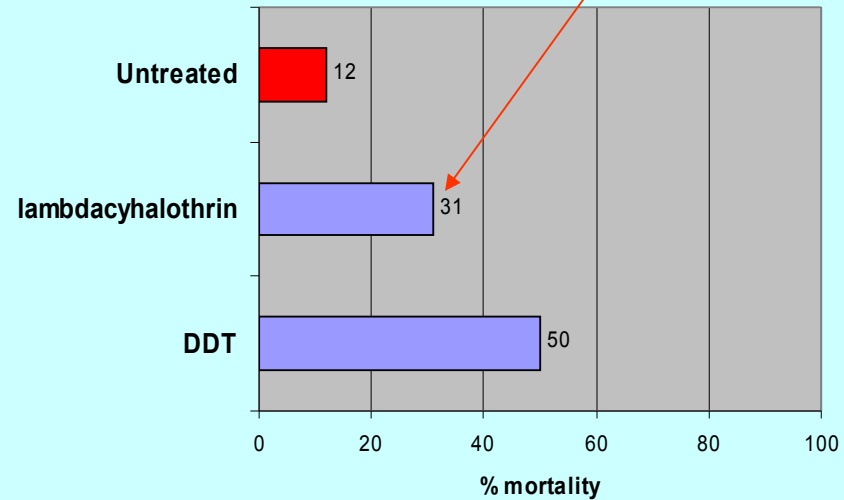
N Benin

Transmission control



S. Benin

Transmission control lost?



pyrethroid susceptible, DDT resistant
GST transferase

Pyrethroid and DDT resistant
Kdr + oxidases

Responding to resistance

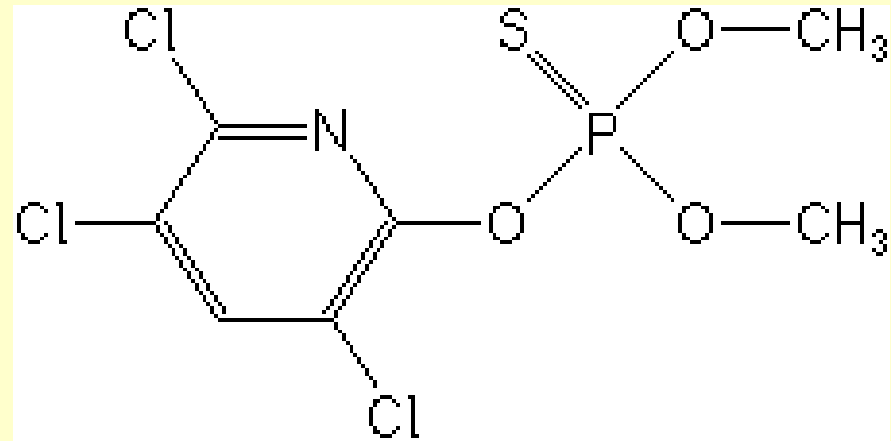
- **Alternative insecticides**
 - **New active ingredients**
 - 10y between discovery and practical use
 - **Repurposed insecticides**
 - Agricultural origin
 - Ingestion and contact action
 - Short lived
 - Slow acting
- **Combination products**
 - Two-in-one ITNs
 - Mixtures of AI on ITNs or IRS
- **Reduce insecticide usage**
 - IVM (cf Integrated Pest Management)
 - Non chemical control
 - Spatial repellents

Repurposed insecticides

- Indoxacarb (oxadiazine)
- Chlorfenapyr (pyrrole)
- Chlorpyrifos methyl (OP)
- Pirimiphos methyl (OP)
- Others

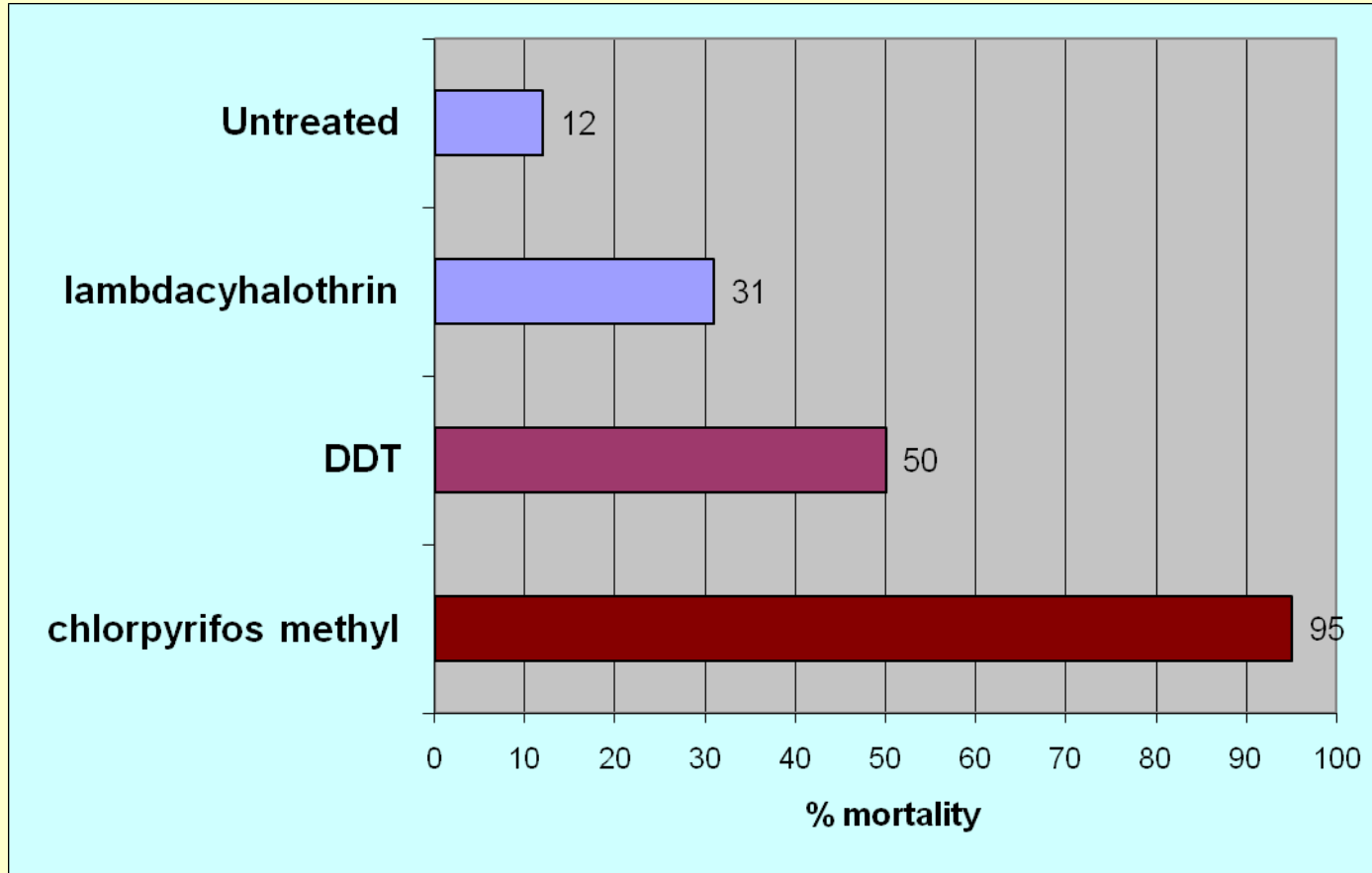
Chlorpyrifos methyl (Reldan CS)

- OP from Dow AgroSciences
- Microencapsulated formulation
 - Prolonged activity as IRS
- Hut trial (IRS) comparing
 - Chlorpyrifos methyl
 - DDT
 - Lambdacyhalothrin



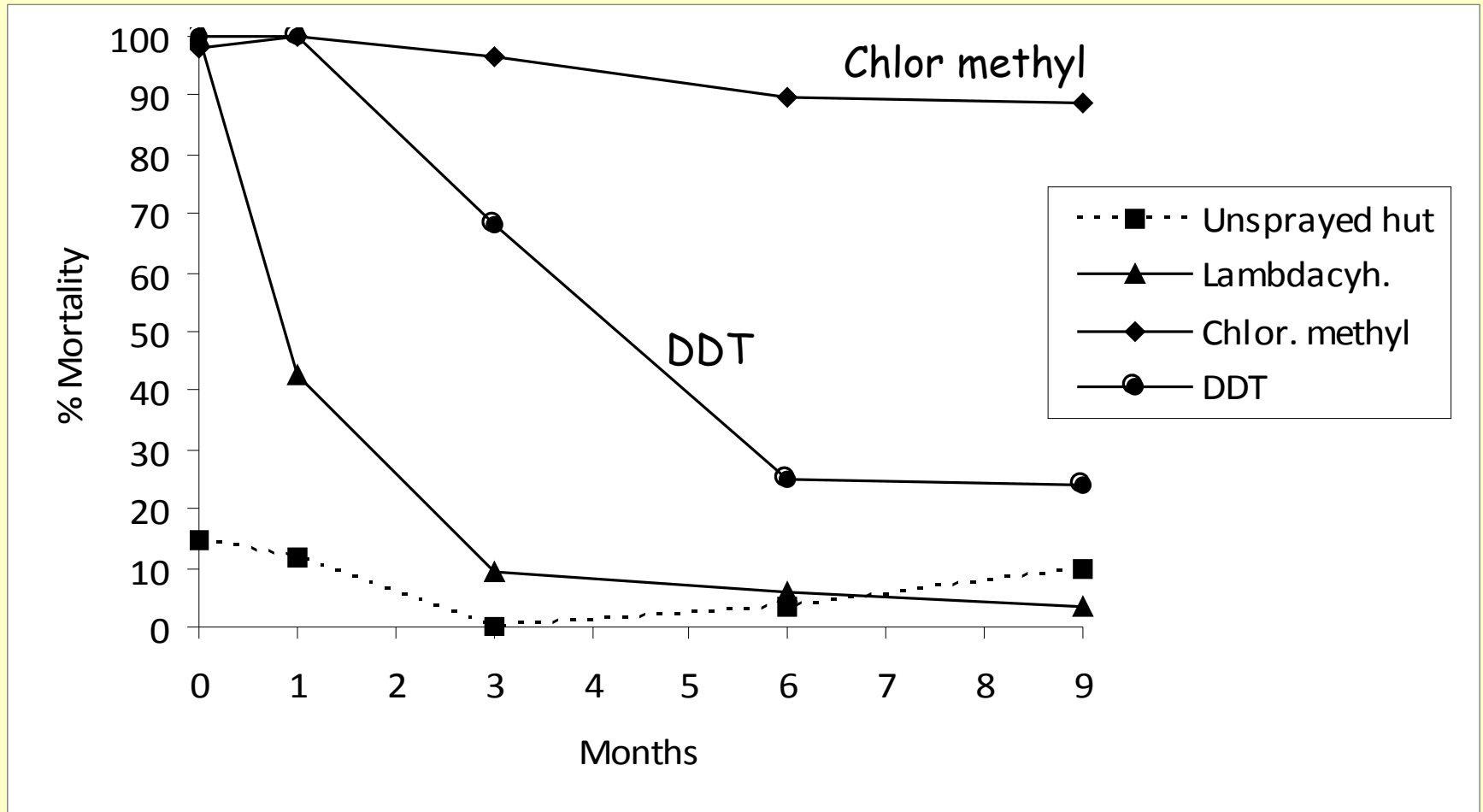
Indoor Residual Spraying

An. gambiae M form (pyrethroid resistant) in S. Benin



***An. gambiae* control restored with chlorpyrifos methyl**

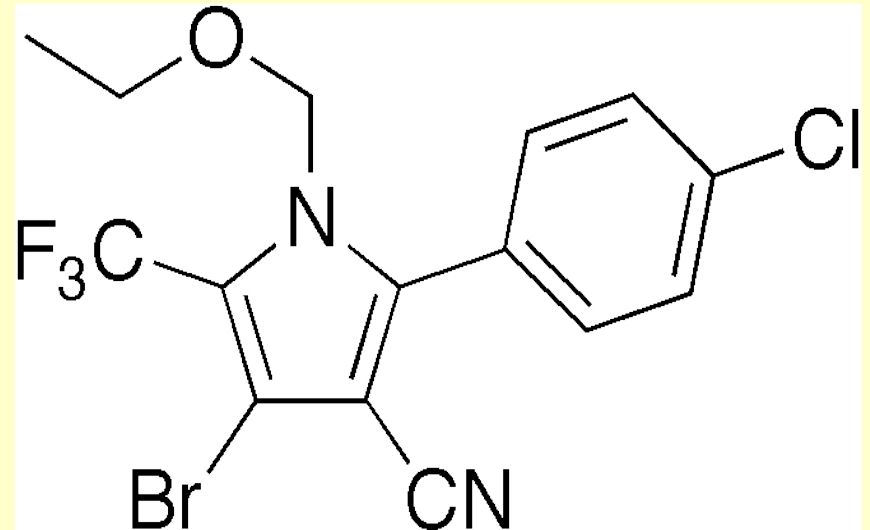
Residual activity of on cement walled huts



- DDT perhaps not so residual, long lasting alternatives are feasible
- Reformulation pragmatic way to repurpose agro-pesticides - quick wins

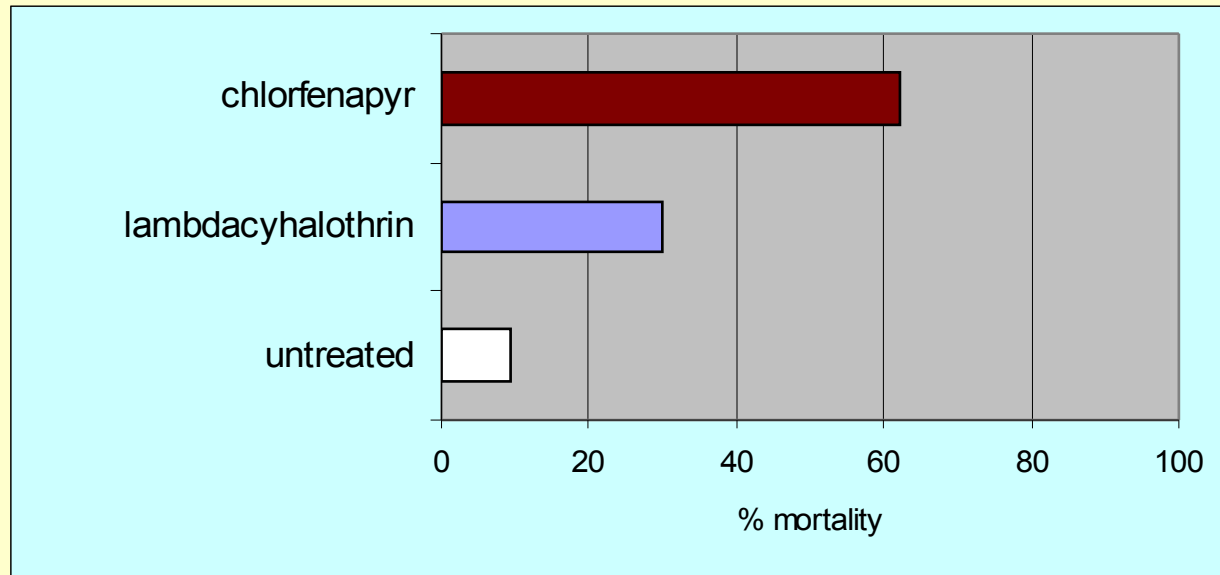
Chlorfenapyr

- Pyrrole insecticide
- BASF
- Non neurotoxic
- METI: disrupts energy transfer in mitochondria
- No cross resistance to pyrethroids or OP/carb
- Low mammalian toxicity

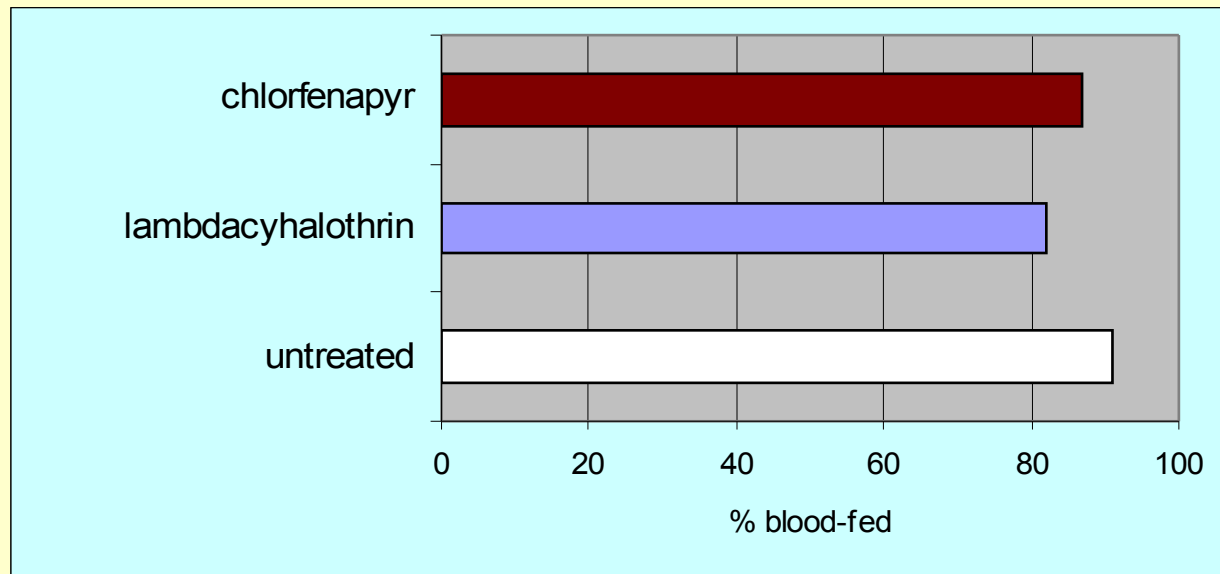


Trials of chlorfenapyr **ITN** against resistant *An gambiae* in S Benin

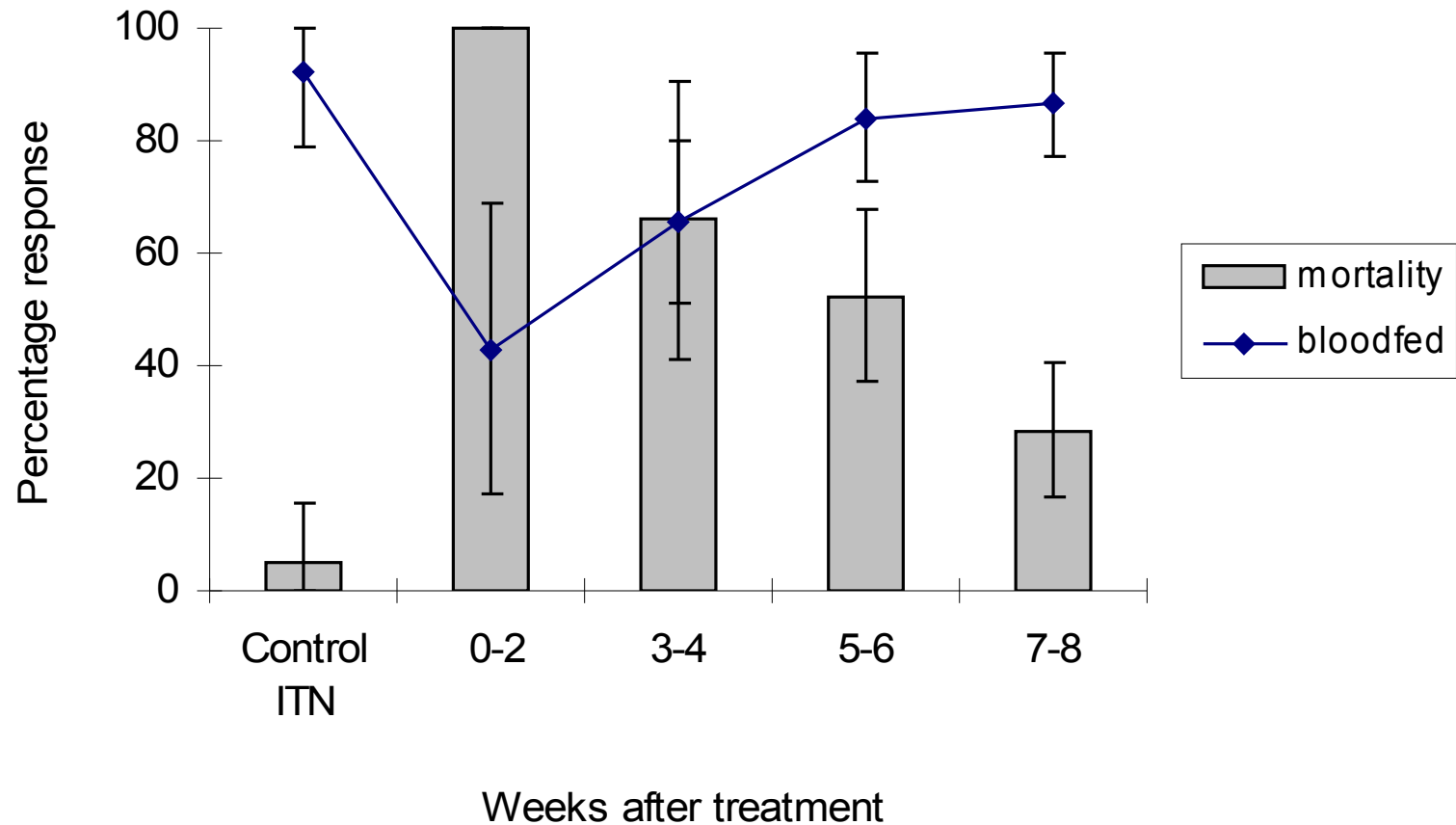
Mortality



Blood-feeding

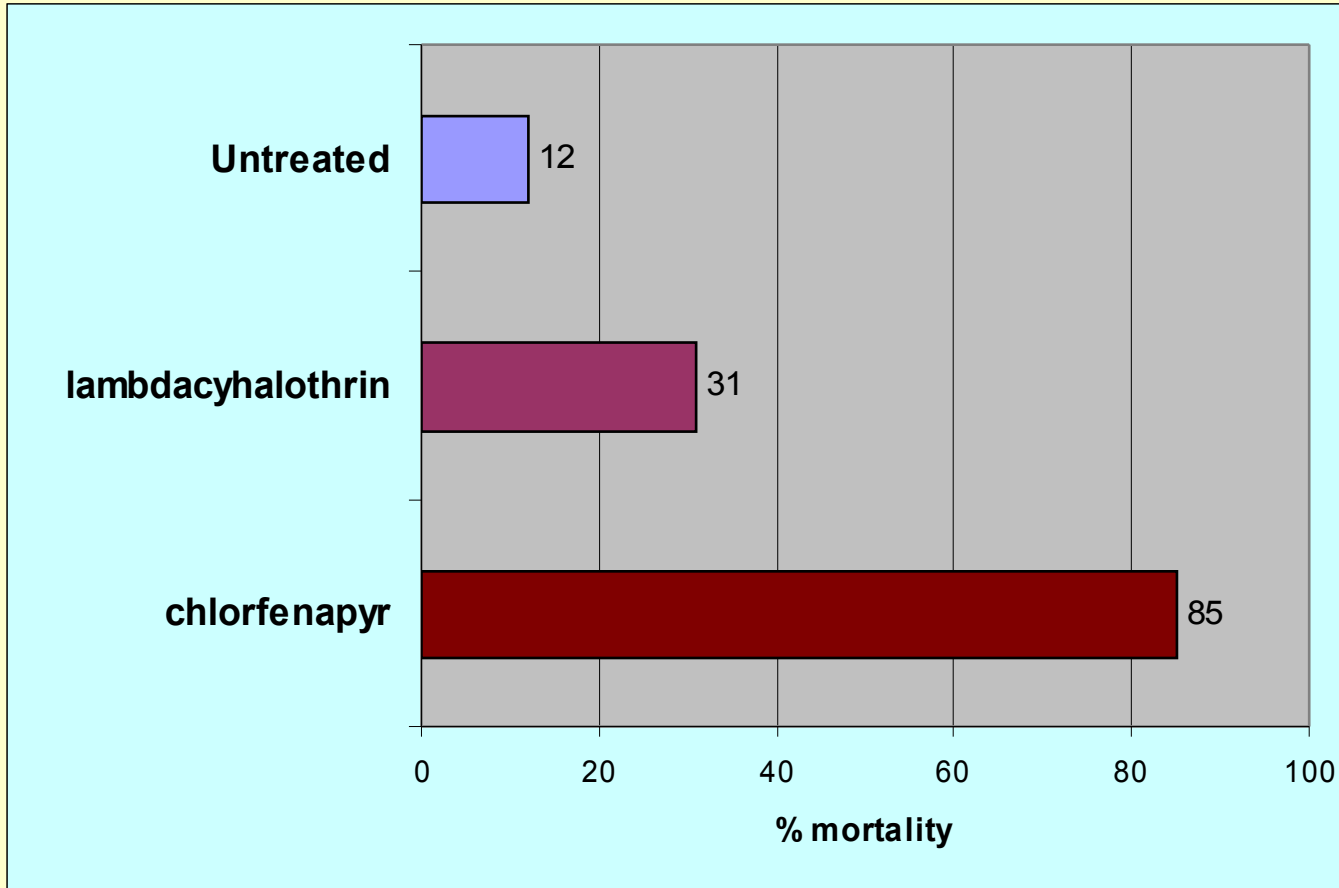


Loss (decay/abrasion) of chlorfenapyr on ITN during the hut trial against *An gambiae*



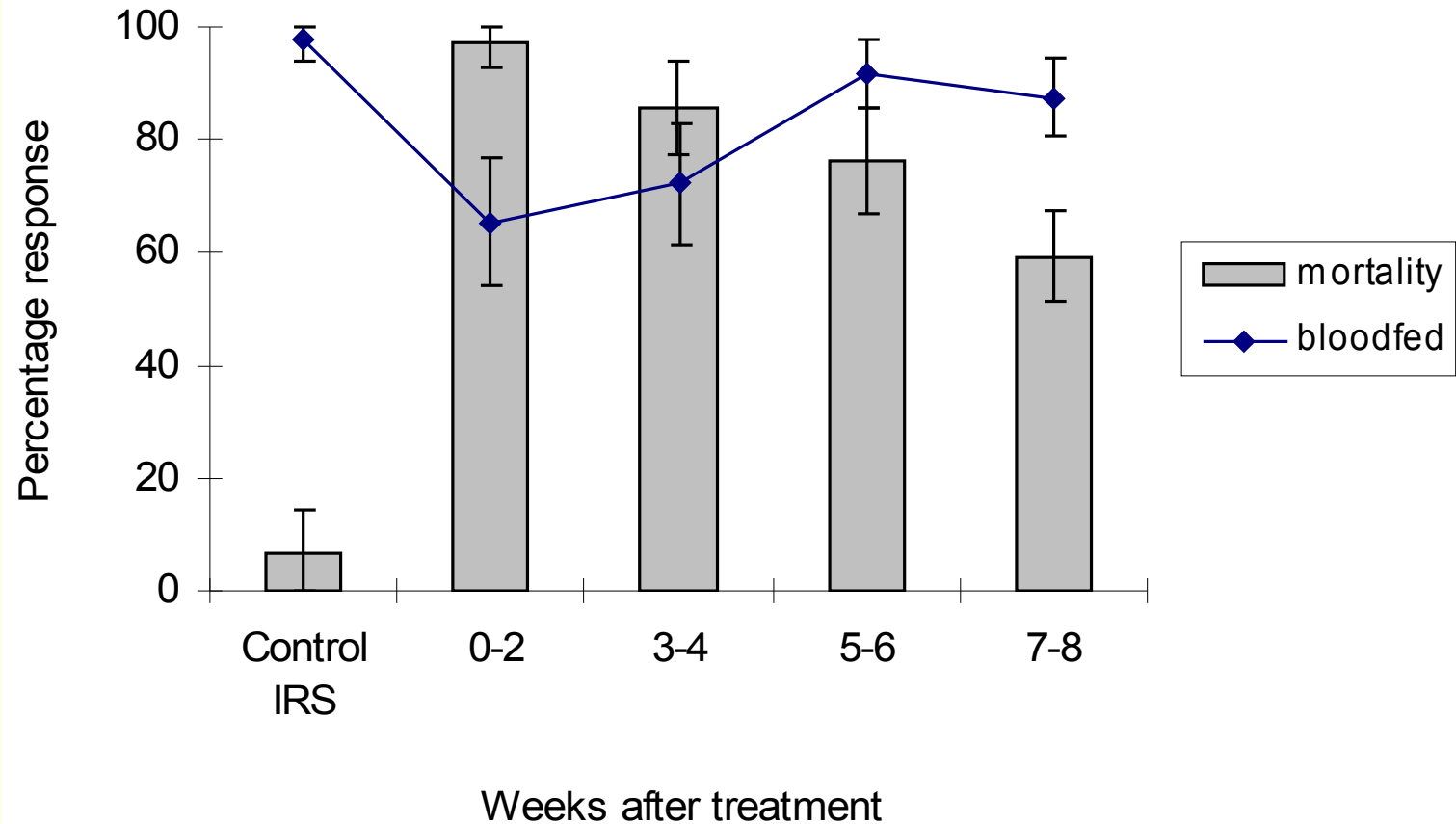
Indoor Residual Spraying with chlorfenapyr SC

Pyrethroid resistant *An. gambiae* in S. Benin



***An. gambiae* control restored with chlorfenapyr**

Decay of chlorfenapyr IRS during the hut trial against *An. gambiae*

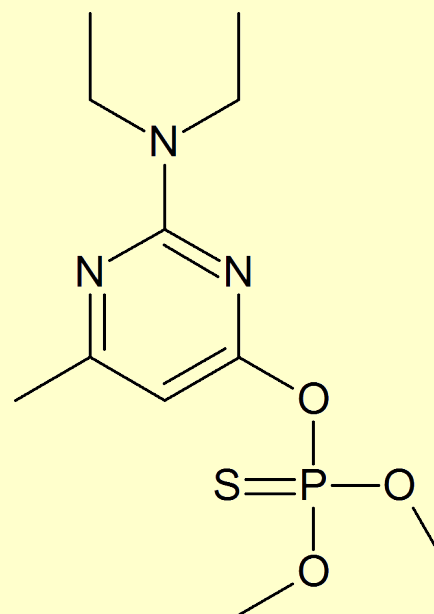


Chlorfenapyr

- AI has potential in vector control
 - IRS
 - LLIN in combination with pyrethroid
- Reformulation

Pirimiphos methyl - Actellic CS

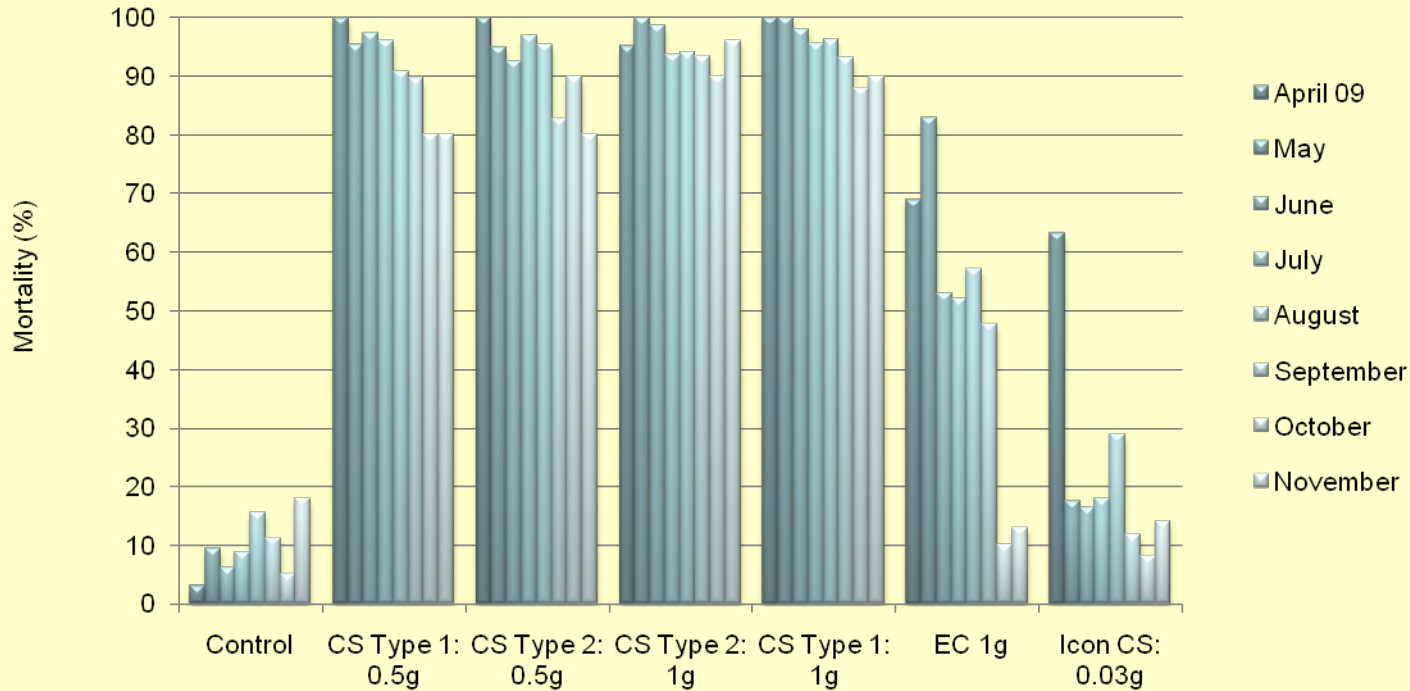
- **Organophosphate, produced by Syngenta**
- **Trials supported by IVCC**
- **Microencapsulated formulation**
 - **Prolonged residual activity**



Treatments and application rates in experimental huts in S. Benin on mud and cement walls

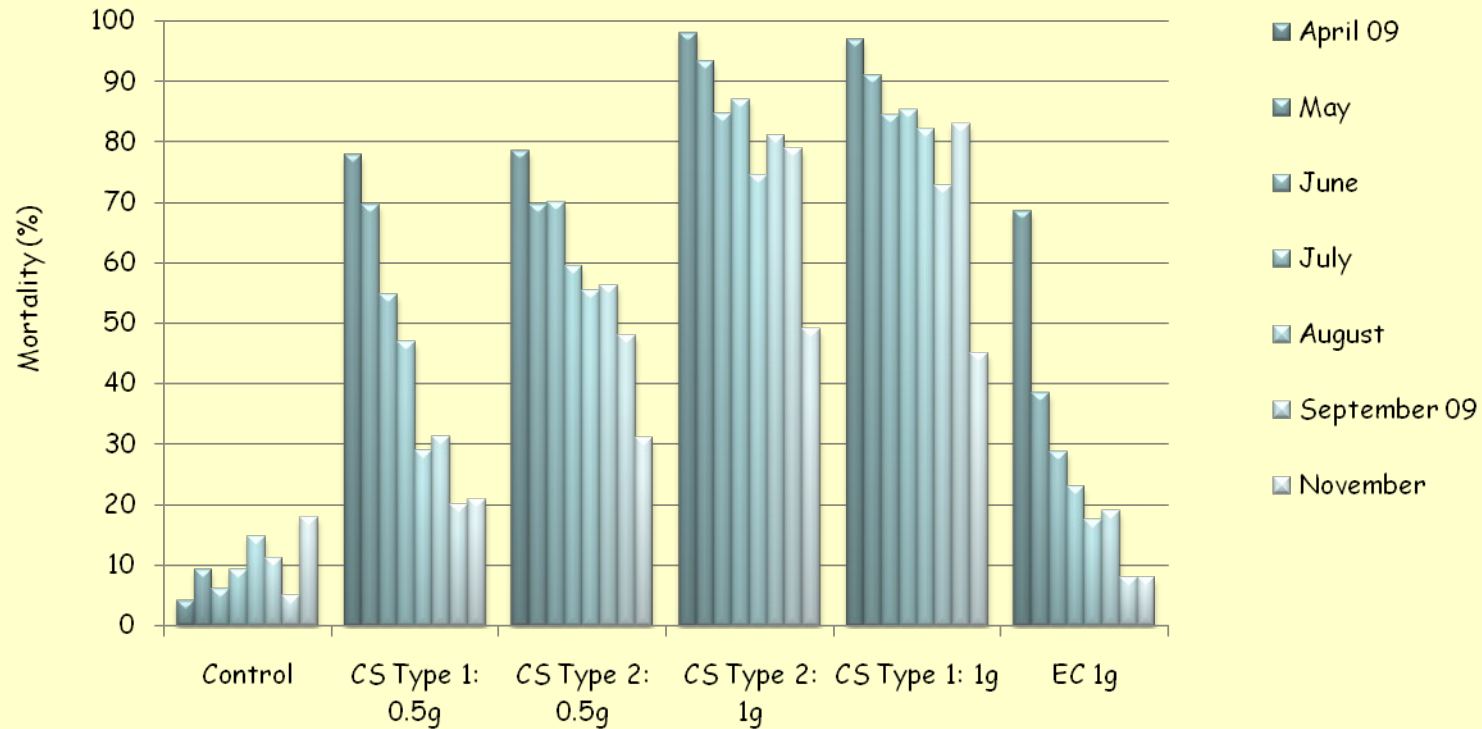
1. Actellic CS Type 1: $0.5\text{g}/\text{m}^2$
2. Actellic CS Type 2: $0.5\text{g}/\text{m}^2$
3. Actellic CS Type 1: $1\text{g}/\text{m}^2$
4. Actellic CS Type 2: $1\text{g}/\text{m}^2$
5. Actellic EC: $1\text{g}/\text{m}^2$
6. Icon CS: $0.03\text{g}/\text{m}^2$
7. Untreated control hut

Efficacy against pyrethroid resistant *An. gambiae* in cement huts



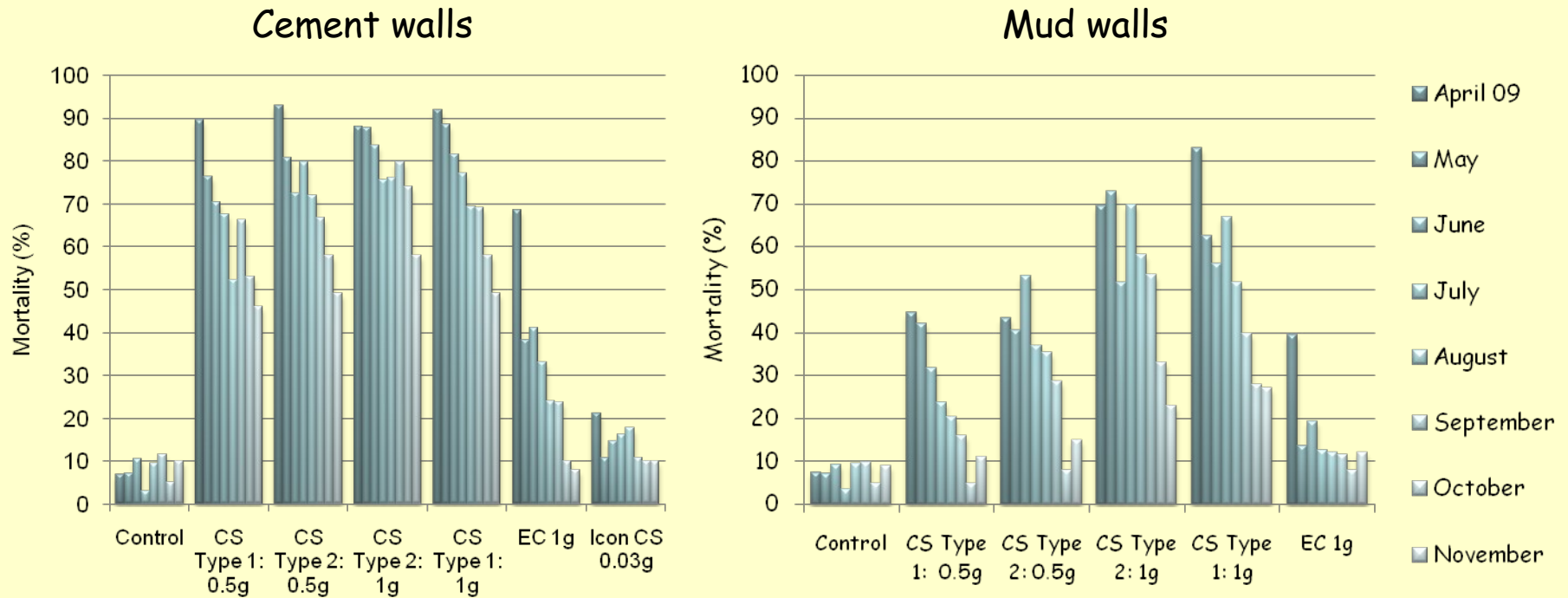
- Actellic CS at 0.5 and 1g/m² kill >80% after 8 months
- Loss of activity with Actellic EC and Icon CS after short time

Efficacy against free-flying *An. gambiae* in mud huts



- Lower mortality on mud than on cement with the lower dosage
- Mortality $\geq 80\%$ after 7 months

Efficacy against free-flying *Cx. quinquefasciatus* in huts



- High mortality against *Culex* for >6 months

Combination products

- Analogous to combination drugs (ACTs)
- AI with complementary properties
 - Pyrethroid fast acting, potent against susceptible forms
 - Slow acting AI or synergist to kill resistant forms
- Combination LLINs
 - Mixtures or two-in-one formats
 - Synergists (PermaNet 3.0 with PBO)
 - Repurposed agro-pesticides
- Combination IRS
 - Alternations in time
 - Mixtures?

Conclusions and needs

- Pyrethroid resistance major threat
- Alternative insecticides exist: some old, some new, both drawn from agropesticides
- Reformulate for LLINs or IRS to improve residuality or wash resistance
- Accelerate development and evaluation of combination products

Acknowledgements

LSHTM

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M Colfeldt

Bayer

V Gutschmann, K Horn

IVCC

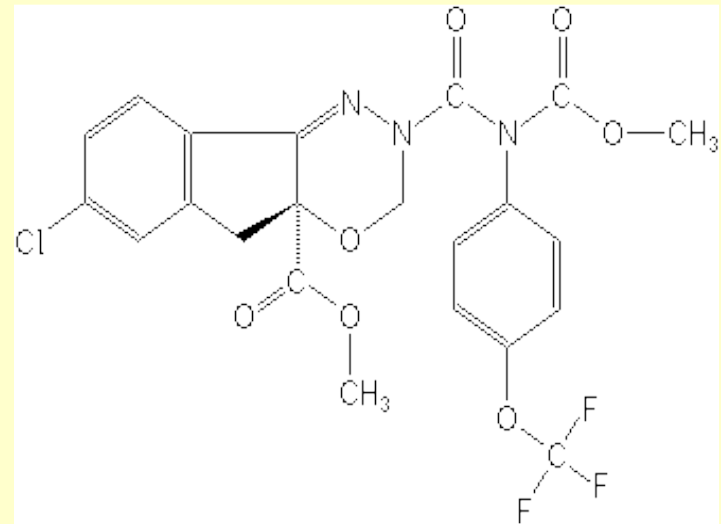
R Sloss, D Malone, T McLean, J Hemingway

Indoxacarb

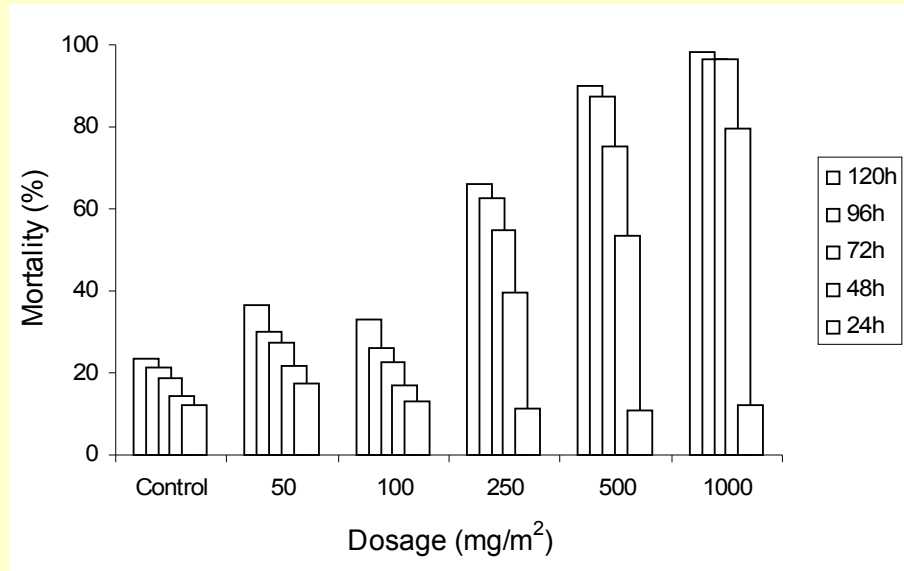
Oxadiazine from Dupont

Acts on Na⁺ channels

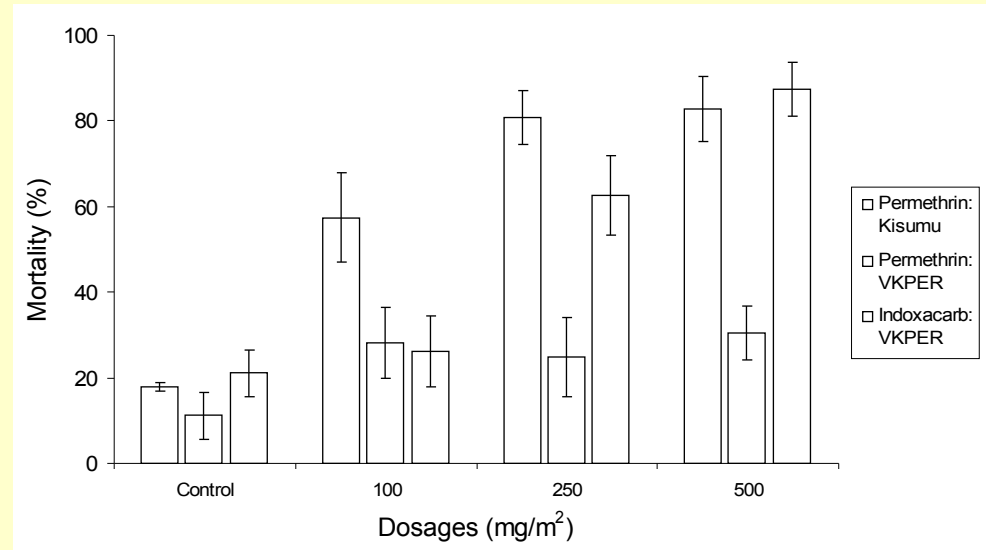
No cross resistance to pyrethroids or OPs



Indoxacarb activity on netting



Slow acting



More active than permethrin against resistant *An. gambiae*