RBM Vector Control Working Group

4th Optimizing Evidence for Vector Control Interventions Work Stream Meeting

Tuesday 7th February 2012
IFRC Auditorium, Geneva, 15:30-18:30

Co-leaders: Prof. Christian Lengeler & Dr. John Gimnig
Rapporteur: Dr. John Silver

Durable Wall Linings – Dr. John Gimnig

The presentation described a CDC randomized trial of insecticide-treated wall linings in western Kenya. The study was conducted in six pairs of villages, with one village in each pair randomized to receive wall linings. All households had ITNs. 1700 house structures were fitted with wall linings. There was no evidence of pyrethroid resistance at the start of the study. Adjusted protective efficacy of wall linings and ITNs against ITNs alone was 38% overall, 31% in children aged 6 months to 4 years, and 42% in children aged 5-14 years.

Participants were also informed that a study on durable wall linings planned to commence in Liberia had been stalled due to detection of high levels of pyrethroid resistance, in spite of an absence of vector control for many years. It is expected that the trial could recommence within 12 months with a non-pyrethroid insecticide.

Discussion

It was suggested that the reported effects of the Kenya study may be somewhat conservative, given that the study villages are small and close to each other.

It was acknowledged that the future of durable wall lining products treated with deltamethrin is likely to be limited; however it is important that trials continue in order to obtain proof of concept and support the development of guidelines and indicators prior to introduction of wall linings as a new category of intervention.

Spatial and Individual Repellents – Dr. Sarah Moore

Results of studies to determine the potential for use of repellents as a complementary intervention to address residual malaria transmission were presented. Results of trials of topical repellents in Pakistan, Bolivia, Peru/Ecuador, Thailand and Tanzania are variable, with significant protection reported in Pakistan (*P. falciparum* and overall malaria) and Bolivia (*P. vivax* only).

As a result of the difficulties of ensuring compliance and correct use of topical repellents, spatial repellents may ultimately be a preferable option. The presentation described the aims and objectives of the Advancing Repellents to Recommendation (ARR) team, as follows:

Aim: To attain formal acceptance and recognition for the use of spatial repellent strategies from global health authorities as a valuable vector control tool for disease transmission intervention, by providing the evidence needed for decision making

Objective 1. Document spatial repellency (SR) as an effective mechanism of action for vector control
Objective 2. Demonstrate a spatial repellent will impact disease at community level

Results of a recent trial in China of transfluthrin coils alone, or in combination with LLINs against both *P. vivax* and *P. falciparum* were presented, showing good protective efficacy.

	Control	Coils	LLINs	Coils + LLINs
P. falciparum Incidence (1000 person years)	6.45	1.46	0.55	0.36
Odds Ratio of being *P. falciparum* positive (95% Confidence Interval [CI])	1	0.23 (0.10, 0.49)	0.09 (0.03, 0.28)	0.05 (0.01, 0.23)
Age-adjusted OR (95% CI)	-	0.23 (0.11, 0.50)	0.09 (0.03, 0.28)	0.06 (0.01, 0.23)
p-value§	-	0.0002	<0.0001	<0.0001
Protective efficacy (95% CI)	-	77% (50, 89)	91% (72, 97)	94% (77, 99)
P. vivax Incidence (1000 person years)	7.00	1.46	1.66	0.53
Odds Ratio of being *P. vivax* positive (95% Confidence Interval [CI])	1	0.20 (0.09, 0.44)	0.21 (0.10, 0.47)	0.07 (0.02, 0.24)
p-value	-	<0.0001	0.0001	<0.0001
Protective efficacy (95% CI)	-	80% (56, 91)	79% (53, 90)	93% (76, 98)

§ P-values for unadjusted and age-adjusted odds ratios were identical.

Outdoor Malaria Transmission and Repellents – Prof. Marc Coosemans

The design of a study to determine the added value of repellents to LLINs for malaria control / elimination in Cambodia was presented. The study includes entomological, epidemiological and social science components.

Added Value of Combining IRS and LLINs – Dr. Sarah Moore

Results of an experimental hut trial in Tanzania were presented. Combining LLINs and IRS tended to increase the number of mosquitoes collected in exit traps, except in DDT sprayed huts. Icon Life was the most effective LLIN, killing twice as many mosquitoes (adjusted analysis). Actellic ™ was the most effective IRS insecticide with excellent overall mortality (adjusted analysis). There was limited extra advantage of combining LLINs with DDT; however, combining untreated nets with DDT was advantageous. These entomological results are in agreement with clinical data that show >50% less risk of malaria among those using LLINs and living in sprayed houses, relative to those living in sprayed houses but not using nets, as reported in Bioko and Zambezia:

Bioko: Bendiocarb IRS + deltamethrin LLINs; OR = 0.46, (95% CI = 0.76–0.81)
Zambezia: DDT IRS + Olyset or PermaNet; OR = 0.34 (95% CI = 0.21–0.56)

IRS and LLINs in combination in Tanzania – Dr. Mark Rowland

Results of a study being conducted in Muleba district in rural Tanzania was presented

Study design

	Year 1: Baseline	Year 2: Intervention
Arm A	IRS+LLINs	IRS+LLINs
Arm B	IRS+LLINs	LLINs

Hypothesis
The two study arms will show equivalence (non-inferiority) in terms of malaria prevalence and anaemia.

The primary outcomes include: Prevalence of malaria infection in children 0.5-14 years and Mean haemoglobin (g/dL) in children under 5 years. The secondary outcomes include: EIR, vector density, insecticide resistance; Perception, acceptance and usage of LLINs and IRS; Seroconversion rate.

Preliminary results from the pilot and baseline surveys indicate relatively high levels of parasite prevalence (23% in July), despite IRS coverage of 95% and ITN coverage of 93%. Insecticide resistance testing revealed the following mortality data in *Anopheles gambiae* s.l. across clusters:

0 to 38% to lambdacyhalothrin
12 to 40% to DDT
11% to permethrin (tested in 1 cluster only)
72 to 90% to the carbamate bendiocarb
As a result of high resistance, bendiocarb is being used in year 2 of the study.

Discussion

It was noted that in the 2nd year of the study, the IRS compound is changing from lambda-cyhalothrin to bendiocarb and then IRS is being withdrawn. This will make it more difficult to disentangle the results of these two changes.

Update on Effectiveness of Combined Vector Control – Dr. Immo Kleinschmidt

The design of a two-arm study comparing LLINs with LLINs + IRS in Sudan was described. Initially, the study was designed as a three-arm study, but the IRS alone arm had to be removed following a universal coverage LLIN distribution campaign. Randomisation was restricted to ensure that the study arms were balanced on the following cluster specific indicators: baseline prevalence of infection, existing ITN use, kdr frequency, cluster population size and proximity of health facility (y/n)
66 clusters (33 in each study arm) have been randomly selected as sentinel clusters for collecting phenotypic insecticide resistance data. Preliminary data indicate 1,242 confirmed malaria episodes from 6,021 person years of follow-up, with an overall incidence of 206 per 1000 person years. Overall reported net usage by cohort members is 86%.

Steve Lindsay very briefly described a new trial being undertaken in the Gambia. The trial will be a two-arm study comparing LLIN and LLIN + DDT IRS. 73 village clusters have been selected with 2km separation between villages. 7800 children aged 6 months – 13 years have been recruited and LLIN and IRS coverages are at 80% and 90% respectively. Initial data are due next year.

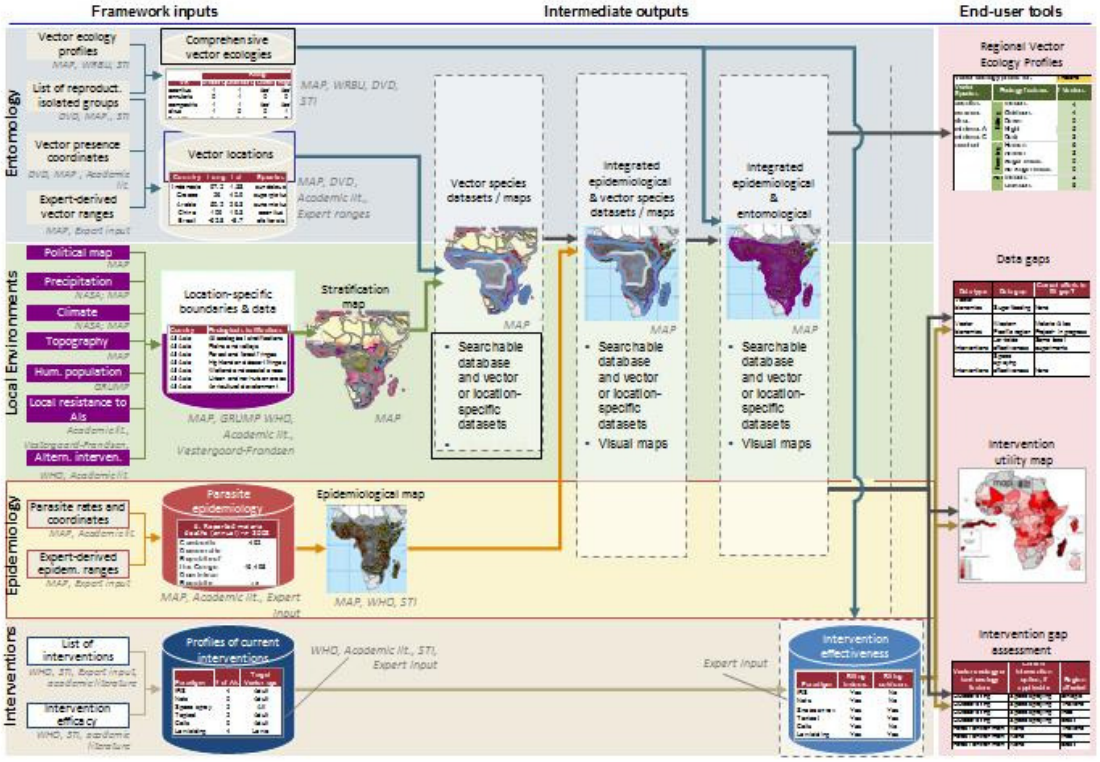
Discussion

Participants acknowledged that the preliminary results from these trials show promise, but the next step is to move towards providing appropriate guidance to national programme managers on how to implement this combination intervention. This needs to be included in the work stream work plan.

Vector Ecology and Control Network VECNet – Dr. Tom Burkot

Tom Burkot described the composition and goals of VECNet. VECNet is a consortium of institutions to analyze malaria transmission and its reduction by one or several vector control interventions. The goals are to:

1. Establish a Digital Library of malaria-specific data
2. Establish an Integrated Modeling Platform
3. Analyze data to estimate the potential impact of vector control tools on a spatially explicit scale



VECNet will comprise data on entomology, environment, epidemiology and interventions and will incorporate several end-user tools to facilitate detailed analysis at different geographical scales. Participants were invited to contribute data to the VECNet Digital Library and use the data to run simulations.

New Intervention Paradigms – Dr. Tom McLean

Tom McLean presented on the work of the IVCC towards developing a framework for validation of new intervention paradigms and product categories in vector control interventions. The purpose of the framework is to: guide our thinking and that of our collaborators, stakeholders and funders as to the type and scale of evidence, supporting activities and technology development at each stage of the

development of new vector control intervention paradigms and product categories in order for new ideas to grow efficiently from concept to established intervention.

The distinctions between intervention paradigms, product categories and products were described, followed by a description of the stages in development of a new product, namely:

- Development of Intervention Concept and Draft TPP
- Proof of Concept
- Verification of Epidemiological Efficacy and Confirmation of TPP
- Policy Endorsement and Product Category Adoption

Discussion

It was proposed that in future, wherever a randomized control trial is conducted, it should include an economic analysis. At early stages of product development, the intervention is often not economically cost-effective, as was the case with LLINs initially. However, use of robust economic analysis would show that costs could potentially be brought down over time, or that benefits are sufficiently long-lived to enable amortization of costs over a sufficiently long period. If the benefit is large enough, then donors could potentially step up even where costs are initially considered to be 'too high' (e.g. the case of switching from CQ to ACTs).

It was noted that there are two key opportunities for donors to intervene in the development process, namely at the R&D stage, and in post-production funding. There are whole series of new formulations and novel products in pipeline that would not have been possible without use of donor money to absorb risk at early stage. On track to develop 3 totally new chemical modes of action by 2020. Exciting.

Manufacturers expressed some concerns that there are already enough rules out there inhibiting manufacturers from bringing new technologies to market and that a new framework was not required. In response it was stated that the framework is designed to offer a process to facilitate a smooth and more rapid transition to a WHO policy statement, which is ultimately what we all want to see.

Key Issues

- High levels of LLINs everywhere means it is no longer possible to have an IRS-only comparison group; major implications for all new Vector Control products
- Fast development of resistance to pyrethroids has significant implications for IRS study arms (not much we can do in relation to LLINs)

Final Conclusions and Summary – Dr. John Gimnig

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Actions and 2012 Work Plan

1. Consensus statement on the combination of LLINs with IRS
2. Follow up progress with current studies /trials and determine when appropriate to present review of the work
3. Continued involvement in development of IVCC framework for new VC paradigms
4. Participation in wider efforts to shape VC development pipeline initiated by WHO/GMP
5. Assess significance of rapidly developing resistance to pyrethroids for the testing of new VC tools
6. Harnessing the power of modeling for answering specific questions on evidence of impact of new VC interventions and/or their combination

Agenda

	Topic	Chairs	Time allocated (min)
15.30-15.40	Welcome and overview	Christian Lengeler John Gimnig	10
15.40-16.00	Recent developments in Durable Wall Lining	John Gimnig	20
16.00-16.20	New paradigms: spatial and individual repellents	John Gimnig	20
16.20-16.30	LLIN-IRS interactions – a brief update	Christian Lengeler	10
16.30-16.40	New developments: VECNet	Tom Burkot	10
16.40-17.10	A framework for the validation of new paradigms in vector control – with discussion	Tom McLean	30
17.10-17.40	Interactions and functional relationship with IVCC	Christian Lengeler Tom McLean	30
17.40-18.00	How can we contribute to identifying new and promising VC tools?	Christian Lengeler John Gimnig	20
18.00-18.30	Work plan for 2012	All	30
	Total time		**180 min**

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