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Challenges Facing Malaria Vector Control and Sustaining the Gains To-date: *The case of LLINs*

Alliance for Malaria Prevention (AMP) Meeting
Geneva, 26 January 2015

Malaria Vector Control Unit

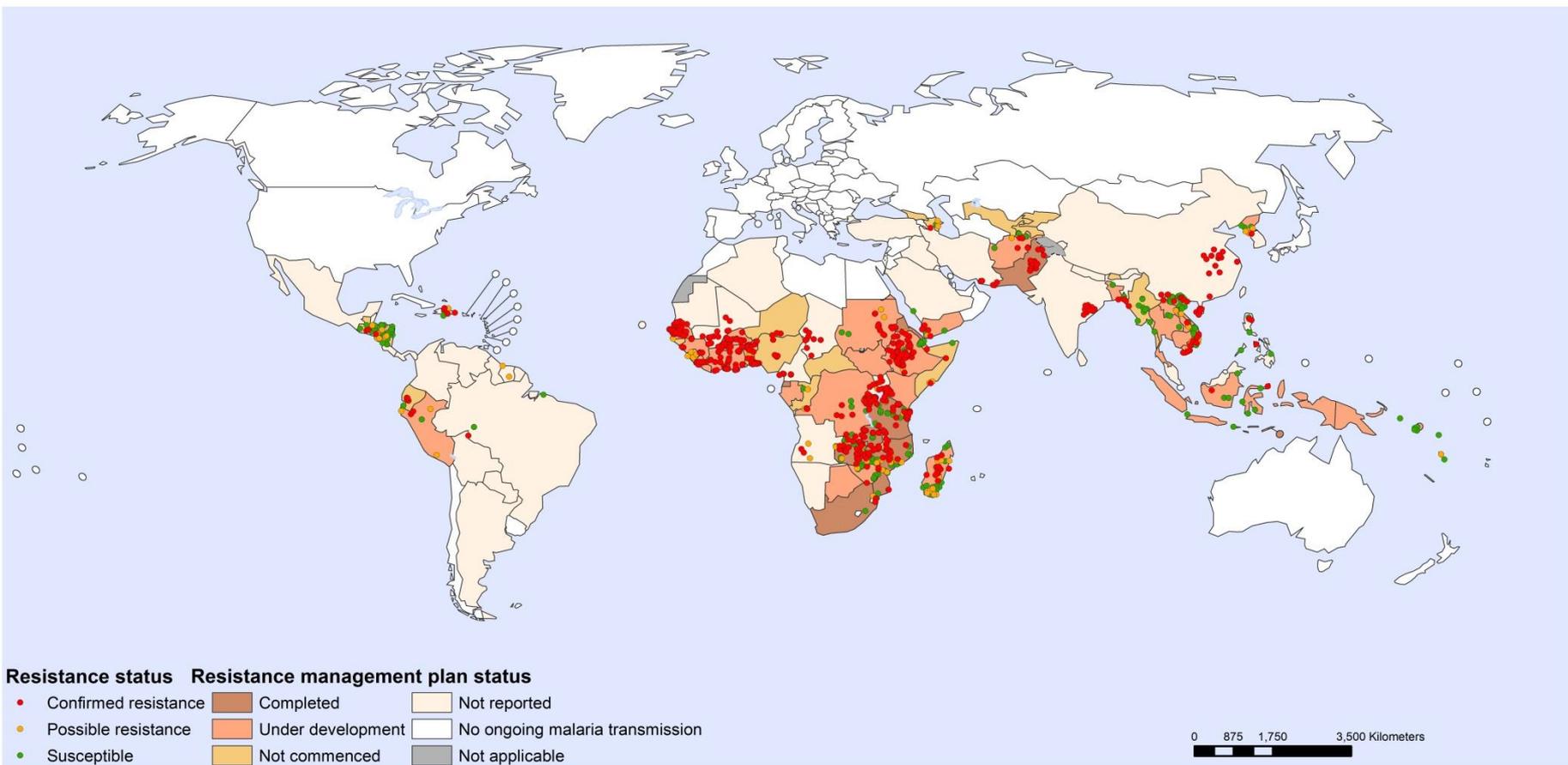
Insecticide Resistance and Global Tracking

GPIRM implementation: some progress

- Insecticide resistance in *Anopheles* has increased at an alarming rate - particularly for pyrethroids
- *Some progress* has been made in implementing GPIRM technical recommendations
- But adoption to policy and operational implementation at country level have generally been poor due to a lack of political will coupled with major financial, human and infrastructural resource deficiencies
- Urgent efforts are needed to ensure correct use of existing interventions and availability of new tools in order to **maintain the effectiveness of malaria vector control**

MPAC Background document. Update on the implementation of the Global Plan for Insecticide Resistance Management in malaria vectors, 10-12 September 2014, Geneva, Switzerland

Reported insecticide susceptibility status for malaria vectors (2010-2014) and status of national insecticide resistance monitoring and management plan (2014)



Where multiple insecticide classes or types, mosquito species or time points were tested, the highest resistance status is shown.

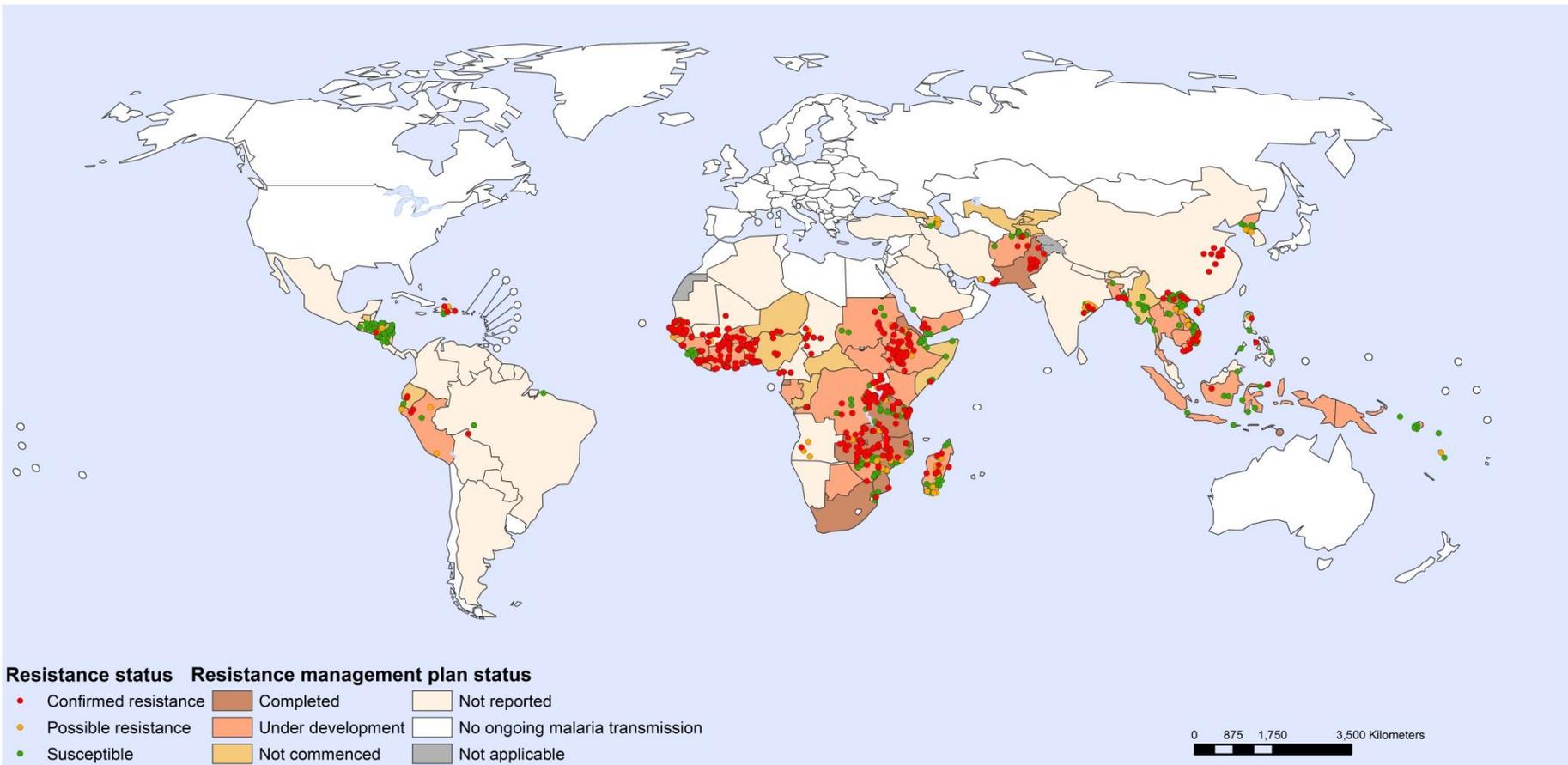
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Malaria Report 2014
Map Production: Global Malaria Programme
World Health Organization



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Reporting and mapping: Challenges

- Data quality
 - No established comprehensive national IR monitoring plan
 - Limited expertise to support data collection – especially for mechanisms
 - Inconsistencies in testing procedures
 - Incomplete or inaccurate data recording or entry
- Data management
 - Lack of an established national insecticide resistance database
 - Limited personnel to manage available information
 - Complicated and overlapping data that are not easy to summarize
 - Sparse or incomplete data which precludes identification of trends
- Data sharing
 - No efficient mechanism for disseminating up-to-date information between partners (*lack of a national technical committee coordinated by NMCP*)
 - Misconception that sharing of data will limit publication opportunities
 - Late or incomplete reporting to WHO

Future WHO plans to address global tracking of insecticide resistance

- Support to countries for development of national insecticide resistance monitoring and management plans
- Inclusion of additional mechanisms data in global database
- Development of online interactive platform for mapping country-level resistance data
- Development of add-on tool to support mapping of national resistance data
- With partners to support countries to build capacity in monitoring and management of insecticide resistance and in vector control broadly

Update on new tools: Progress and challenges

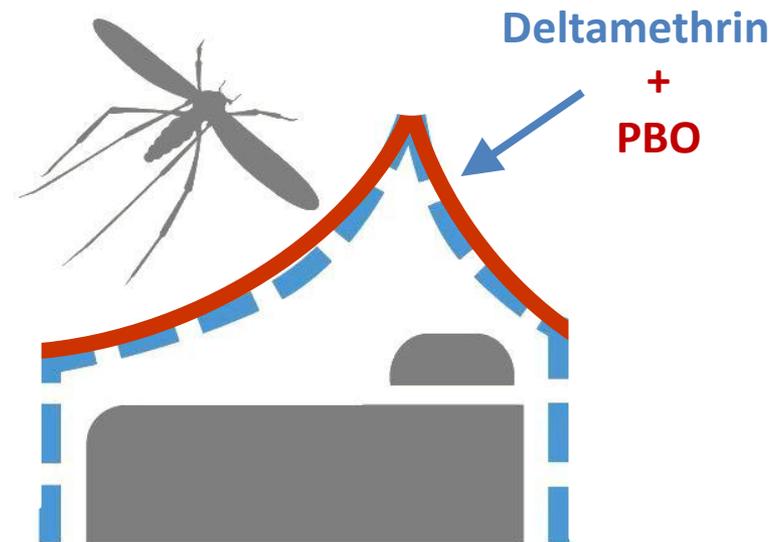
Vector control interventions for pyrethroid resistant areas

Description of paradigm:

- a novel intervention or an adaptation of an existing paradigm.
- reduces vectorial capacity
- reduces infection/disease in humans in areas where the local vectors have substantive pyrethroid resistance

Prototype: Permanet 3.0

- combination LLIN
- sides: deltamethrin only
- top: deltamethrin + piperonyl butoxide (PBO)



PBO is a synergist that enhances effects of pyrethroids by inhibiting metabolic detoxification enzymes

Vector control interventions for pyrethroid resistant areas

Prototype claims: in areas of high pyrethroid resistance,
PBO + pyrethroid = ↑ mosquito death & ↓ human infection

Supporting evidence:

Percentage improvements with PN3 compared to pyrethroid only LNs

Reference	Page # in dossier	Country	Site	Outcome measure	% improvement observed with PermaNet® 3.0
Adeogun et al (2012b)	16-24	Nigeria	Ikorudu	% increase in mortality, relative to Olyset®	26
			Kainji		24
Koudou et al (2013)	26-43	Ivory Coast	Bouaké	% increase in mortality cone test on roof with wild mosquitoes after 12 months use, relative to PermaNet® 2.0	63
			Tiassalé		36
Stiles-Ocran (2013)	44-71	Ghana	Chirano area	% reduction in density (measured by indoor resting catches) from baseline to post-intervention, relative to PermaNet® 2.0	39-84
				% reduction in density (measured by human landing catches) from baseline to post-intervention, relative to PermaNet® 2.0	25-63
Awolola et al (2013)	72-92	Nigeria	Ogun State	% reduction in mean household density, relative to PermaNet® 2.0	27
				% increase in mean mortality, relative to PermaNet® 2.0	56
				% increase in EIR reduction, relative to PermaNet® 2.0	28
Adeogun et al (2012a)	94-107	Nigeria	New Bussa	% increase in mortality from 0 washes to 20 washes, relative to Olyset®	36-43
				% increase in blood feeding inhibition from 0 washes to 20 washes, relative to Olyset®	17-24

Recommendations for the prototype:

- VCAG supported the manufacturer's claim of increased bio-efficacy compared with pyrethroid only LLINs in areas where mosquitoes have metabolic resistance mechanisms
- WHOPES phase 3 evaluation towards full recommendation should be completed
- Any implementation should include resistance monitoring of mechanisms of resistance

Vector control interventions for pyrethroid resistant areas

VCAG Recommendations for the paradigm:

- More data is needed on the impact of pyrethroid resistance on human health.
- Need for guidelines on the minimum data to substantiate claims of efficacy for LLINs targeting areas of high insecticide resistance
 - Guidelines were finalized in November 2014 and are *in the process of publication*

Further, in November 2014, VCAG recommended that:

1. The paradigm of combination nets designed to have increased efficacy in areas of high pyrethroid resistance have a public health value
 - This decision is the basis of a recommendation to MPAC in March 2015 on this paradigm
2. A sub-group of VCAG will carefully evaluate and refine manufacturers claims. Substantiated claims will only then be supported by VCAG

VCTEG proposed recommendations for MPAC's consideration

- These are indeed a new paradigm and new products with different AIs are urgently needed (the ACTs of vector control)
- In the absence of data reflecting different insecticide resistance scenarios, it is not possible at this point to provide guidance on where such nets should be distributed
- An independent review of existing data and/or implementation of decisive trials, to define operational conditions is needed
- While current VCAG recommendation may not in all cases shorten the process of getting new products to market, such nets should at a minimum pass a WHOPES interim recommendation and minimum quality standard

LLIN Durability Studies:
Are results sufficient to inform procurement decisions?

Determination of Fabric Strength of Recommended LLINs

WHO Consultation on assessment of the strength and durability of fabric for long-lasting insecticidal nets (20–22 Aug 2014, WHO-HQ)

Purpose: Review WHO laboratory study results from Phase II on fabric strength and flammability of LLINs and propose recommendations

Study objectives:

- 1) Subject WHOPES recommended LLINs to standard tests of textile strength and flammability
- 2) Correlate results with data on physical durability in the field

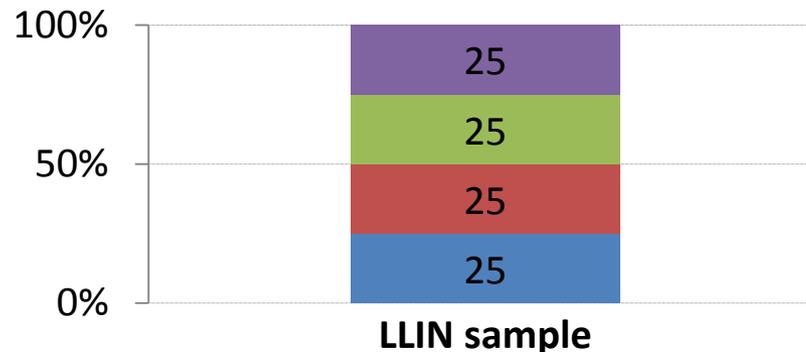
The study was conducted in two phases:

- Phase 1 completed in July 2013, and the results were discussed during the WHO technical consultation on 20–22 August 2013
- Phase 2 included several additional tests for fabric strength and additional LLIN products

Resistance – to – damage values – R4D studies

- Long-term durability depends on the inherent “strength” or resistance of the fabric to damage and the intensity of use in the field
- R4D studies showed that most holes in LLINs in the field are due to mechanical damage, comprising snagging, tearing, abrasive wear and hole propagation
- A “resistance to damage” (RD) score was then calculated from results of four textile tests: bursting strength, snagging strength, abrasion resistance and hole propagation

Aspirational results for an LLIN with an RD score of 100%



Blue, tear resistance; red, snag strength; green, abrasion resistance; purple, hole propagation

Draft Recommendations and Conclusions

The meeting made the following recommendations:

- WHOPES should coordinate inter-laboratory validation of test methods, subject to the availability of funding
- WHO should revise the LLIN specification guidelines to include fabric weight, flammability and other fabric characteristics, after validation of the tests
- WHO should recognize the value of RD scores based on the proposed combination of tests and make the score for each brand of LLIN available
- The RD approach and method should be updated regularly, as new evidence becomes available, and clear mechanisms should be in place to ensure updating and recognition of innovation

Draft Recommendations and Conclusions

- WHO should coordinate multi-centre comparative studies of the durability of LLINs under field conditions with potential support from PMI and GF
- The feasibility and value of a tier system should be revisited once inter-lab validation has been completed
- The global community should invest in evidence-based approaches to promote adequate care and maintenance of LLINs and minimize sources of potential damage
- The capacity of WHO to address these recommendations should be enhanced by additional staff and funding dedicated to monitoring the durability of LLINs.

LLIN Distribution: Financing and local Context

Malaria Financing

	2015	2016	2017
Overall Africa needs and gaps in USD			
Need	3.42 B	3.24 B	3.46 B
Financed	2.38 B	1.69 B	1.12 B
Gap	1.03 B	1.55 B	2.33 B
LLIN commodity gap			
Need	255.6 M	185.4 M	216.9 M
Financed	206.0 M	112.3 M	54.5 M
Gap	49.6 M	74.1 M	162.4 M

In USD: B – billions, M - millions

Sustaining LLIN Coverage

- Mass free LLIN distributions to at-risk populations continue to be necessary
 - Generally every 3 years - assuming routine systems are also functional
- In the absence of functional routine systems, campaigns should occur more frequently than every 3 years
 - Top-up campaigns when population coverage of LLINs of less than 2 years old is greater than 40%
- ANC and EPI - highest priority channels for continuous distribution (before, during and after mass campaigns) - where contact rates are high
- There should be a single National Plan (distribution strategy) under the leadership of the NMCP based on analysis of local context/opportunities/constraints
- A global guidance on prioritization/targeting because of resource constraints is against principles of universal access to health
 - Partners should rather work with individual countries to address short-term gaps as resources are mobilized
 - Analysis of local context requires investing in local capacity

http://www.who.int/malaria/publications/atoz/who_recommendation_coverage_llin/en/index.html

Conclusions

- Insecticide resistance is alarmingly increasing and will compromise our efforts to scale up LLIN implementation
- New tools are urgently needed – including combination nets with two insecticides with different mode of action and with no pre-existing resistance
- Available data on combination nets is not adequate to provide guidance to countries and partners on where to distribute them
- Resistance to damage (RD) scores have the potential to inform future procurement decisions, however, until such scores are validated in different laboratories supported with field data, it may be premature to recommend them
- Sustaining gains in LLIN implementation with local context in mind, would require continued efforts to mobilize resources and **build the capacity of nationals**

Thank you!