WHO Guidance Note for Estimating the Longevity of LLINs in Malaria Control

Malaria Policy Advisory Committee
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Outline

- What are the minimum criteria of LLINs?
- How do we monitor LLIN durability?
- Why is estimating LLIN longevity/survival important?
- Why do we need a technical guidance to estimate LLIN longevity?
- How do we estimate LLIN longevity?
- What are the outstanding issues in estimating LLIN longevity?
- Recommendations for MPAC's consideration
  - Countries
  - Partners
  - WHO
WHO definition of LLINs

- An LLIN is a factory-treated mosquito net that is expected to retain its biological activity for:
  - a minimum number of standard washes under laboratory conditions (= 20)
  - a minimum period of use under field conditions (= 3 years)
Criteria for efficacy of LLINs

- After 20 washes, the netting must produce the following:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cone bioassays</td>
<td>( \geq 80% \text{ mortality and/or } \geq 95% \text{ knockdown} )</td>
</tr>
<tr>
<td>Tunnel test</td>
<td>( \geq 80% \text{ mortality and/or } \geq 90% \text{ blood-feeding inhibition} )</td>
</tr>
</tbody>
</table>

- Efficacy criteria cannot be used for quality control
- Hence the use of physico-chemical criteria in WHO specifications of LLINs
Survival of LLINs in the field is variable

- Two 75 denier polyester nets
- Both 3 years old
- One in good condition and the other too torn

*Photos by Albert Kilian*
WHO (GMP and NTD) Guidelines on Monitoring LLIN Durability
Knitting patterns of LLINs influence durability

Pattern A

Pattern B
Durability Data from Phase III study of an LLIN product in Western Uganda – kindly provided by Albert Kilian
Why is estimating LLIN survival/longevity important?

- Data on LLIN durability could be used to compare performance and therefore influence procurement decisions.
- It is crucial in planning for net replacement in the field.
- Programmes have asked – how long do LLINs actually last?
  - Guidelines exist on monitoring LLIN durability.
  - Programmes have not been collecting this important data routinely.
  - Data available only from a few countries – including those by PMI, R4D and WHOPES phase 3 studies.
Technical Expert Group On Malaria Vector Control
Why is this technical guidance needed?

- What we need is the “median survival” of an LLIN product in a given situation as a measure of durability.
- However, current guidance documents only explain:
  - How attrition (net loss) should be measured,
  - How condition for each surviving LLIN should be assessed and summarized in a “proportionate Hole Index”
  - But not how these are to be combined into one metric.
What are the real issues?

- Need to always combine attrition and physical integrity measures
  - But only include a certain part of attrition
- Categorize pH1
  - To make it more robust
  - To identify those nets still “serviceable”
  - Need to include precision of estimates
    - To show that one product is really performing better than another
Should insecticidal residual efficacy be part of estimating LLIN longevity?

- Review of evidence by the VCTEG recommended not to include insecticidal residual efficacy in estimating LLIN survival until
  - A test is available that can be carried out in the field on all samples without removing or destroying the net
  - There is a better understanding of the minimal insecticidal effectiveness i.e. the level of insecticide at which no additional epidemiological protection is achieved
The Proposed Solution
Data on LLIN Attrition

- Data on attrition should be collected from all studies, retrospective (recall) and prospective

- Main reason for loss need to be differentiated
  - Given away for others to use
    - Family
    - Friends
    - Stolen
  - Discarded or destroyed
    - Accidentally destroyed
    - Thrown away (buried, burnt etc.)
  - Used for other purposes
## Setting a Cut-off for Proportionate Hole Index

<table>
<thead>
<tr>
<th>Category</th>
<th>pH1 value range</th>
<th>Approximate total hole surface area in cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>If circle*</td>
</tr>
<tr>
<td>Good</td>
<td>0-64</td>
<td>&lt;79</td>
</tr>
<tr>
<td>Damaged</td>
<td>65-642</td>
<td>80-789</td>
</tr>
<tr>
<td>Torn</td>
<td>643+</td>
<td>&gt;790</td>
</tr>
</tbody>
</table>

- Create additional category for analysis by combining “good” and “damaged” nets to
  - “serviceable” = pH1 < 643
Categorization of the pH1

- This categorization creates dichotomous variables that are easy to deal with statistically.
- It also increases the robustness of the pH1 result.

![Categorization Diagram]
Estimating LLIN survival – using hypothetical curves

- Calculate “survival to time x”, i.e. at the time of the survey
- Plot time points against hypothetical survival curves and estimate “median LLIN survival” from two or more data points
Survival to time x

- Without insecticidal residual efficacy

\[
\text{% surviving to time } x = \frac{\text{# of LN present and "serviceable" at time } x}{\text{# of LN originally received and not given away at time } x} \times 100
\]
Plot LLIN survival outcomes
Estimating survival of LLINs

- From at least 2 points of which the lowest should be 85% or lower

\[ t_m = t_1 + \frac{(t_2 - t_1) \times (p_1 - 50)}{(p_1 - p_2)} \]

<table>
<thead>
<tr>
<th>Time point</th>
<th>Time in years</th>
<th>Functional survival</th>
<th>Median survival using last two data points (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>93.3%</td>
<td>n.a.</td>
</tr>
<tr>
<td>2</td>
<td>1.7</td>
<td>83.4%</td>
<td>4.1 (3.7 to 4.5)</td>
</tr>
<tr>
<td>3</td>
<td>2.4</td>
<td>68.2%</td>
<td>3.2 (3.0 to 3.5)</td>
</tr>
<tr>
<td>4</td>
<td>3.1</td>
<td>53.2%</td>
<td>3.3 (3.0 to 3.5)</td>
</tr>
<tr>
<td>5</td>
<td>4.3</td>
<td>31.6%</td>
<td>3.3 (3.0 to 3.6)</td>
</tr>
</tbody>
</table>
Example of Nigeria – showing area differences on LLIN survival –

Albert Kilian
Outstanding issues of priority

- Develop standard operation procedures (SOP) for all steps of LLIN survival estimation
- Study relationship between mosquito entry with hole size and position of an LLIN and the influence of total net size compared to hole size
- Study relationship between net damage, remaining insecticide and feeding inhibition in susceptible and resistant vectors in hut trials – help to define cut offs
- Establish the epidemiological impact of damaged LLINs, age and insecticidal levels
- Accelerate the development of field tests that reliably predict protective effectiveness of LLINs
Recommendations for MPAC's consideration
Countries

- Include in country work plans the routine collection of data on LLIN durability
- Analyze available data according to the proposed method of estimating LLIN survival according to the proposed recommendations
- Share the results from LLIN survival analyses with other partners so that a better understanding of the dynamic of LLIN survival can be obtained
- Where sufficiently reliable information exist, include this in their planning for malaria prevention using LLINs – including net replacement
Partners

- Support countries in the collection and analysis of LLIN survival data directly and by also building relevant capacity.
- Undertake research to address outstanding issues identified in this document.
- Actively contribute to the improvement of methods of estimating LLIN survival in the future.
WHO

- WHOPES should consider “proportion of LLINs that survive to three years of field use in ‘serviceable’ condition” as a minimum requirement of LLINs
- Disseminate and promote this document and accompanying tools to countries and partners for use by NMCP where LLINs are a key intervention
- Facilitate the collection, analysis and sharing of results of comparable LLIN survival data by providing resources for training and technical support
- Use existing policy setting mechanisms to regularly review this guidance as new information emerges – including the possibility of ranking LLINs according to their performance
Thank you!