Is there added value of the combined use of spraying and treated nets?

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Relevance

• Interest in the combination of IRS with LLINs stimulated by
  – spread of vector resistance to pyrethroids,
  – variations in the apparent impact of one intervention alone on malaria transmission
  – whether IRS+LLINs combination can help to achieve local elimination?

• Evidence from 4 trials and 17 observational studies
• Most mathematical models predict added effect of the combination
Weighing the evidence

- Well-conducted randomised trials give best evidence
- If designed as superiority trials, the null hypothesis is that combination is no better than LLIN alone. Showing no effect does not prove Ho
- To prove that the combination is equivalent to LLIN alone, need to conduct a non-inferiority trial
- In vector control trials intervention effects might be masked by mosquito movement between villages, or by emerging or undetected insecticide resistance
- Interpretation is complicated by many factors that differed between studies (vector, insecticide, IR, coverage, X-transmission intensity...)
<table>
<thead>
<tr>
<th>Country</th>
<th>IRS Insecticide</th>
<th>Number of clusters/arm</th>
<th>Main vector</th>
<th>Reported LLIN coverage by arm</th>
<th>Reported IRS coverage</th>
<th>Susceptibility of main vector</th>
<th>PfPR&lt;sub&gt;2-10&lt;/sub&gt; Endemcity class&lt;sup&gt;§&lt;/sup&gt;</th>
<th>Primary endpoint Effect [95% CI]&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benin</td>
<td>B-carb</td>
<td>7</td>
<td>A.gambiae s.s. target groups only</td>
<td>&gt;90%</td>
<td>97</td>
<td>High</td>
<td>IRR=1·32 [0·90-1·93]</td>
<td></td>
</tr>
<tr>
<td>Sudan</td>
<td>B-carb</td>
<td>70</td>
<td>A.arabiensis</td>
<td>&gt;95%</td>
<td>Range 43-100</td>
<td>Low</td>
<td>IRR=0.87 [0.54-1.39]</td>
<td></td>
</tr>
<tr>
<td>The Gambia</td>
<td>DDT</td>
<td>35</td>
<td>A.gambiae s.s. &amp; arabiensis</td>
<td>very high</td>
<td>&gt;80%</td>
<td>High but kdr resistance genes reported nearby</td>
<td>IRR=1.08 [0.80-1.46]</td>
<td></td>
</tr>
<tr>
<td>Tanzania</td>
<td>B-carb</td>
<td>25</td>
<td>A.gambiae s.s. A.arabiensis A.funestus</td>
<td>modest</td>
<td>~90%</td>
<td>Range 28-70</td>
<td>Intermediate</td>
<td>OR=0.43 [0.19-0.97]</td>
</tr>
<tr>
<td>Kenya</td>
<td>Pyr</td>
<td>Non randomised</td>
<td>A.gambiae s.s. A.arabiensis A.funestus</td>
<td>very high</td>
<td>74%</td>
<td>Not reported</td>
<td>High</td>
<td>IRR=0.38 [0.28–0.50]</td>
</tr>
<tr>
<td>Burundi</td>
<td>Pyr</td>
<td>Non randomised</td>
<td>A.gambiae s.s. A.arabiensis A.funestus</td>
<td>high</td>
<td>&gt;90%</td>
<td>Not reported</td>
<td>Intermediate</td>
<td>OR=0.88 [0.60-1.31]</td>
</tr>
</tbody>
</table>

<sup>§</sup> Susceptibility class indicates the level of resistance:
- Very high: 95% or more of the population is susceptible.
- High: 80% to 94.9% of the population is susceptible.
- Intermediate: 60% to 79.9% of the population is susceptible.

<sup>d</sup> Primary endpoint effect (IRR) is calculated as the ratio of two groups (usually control vs. intervention).

Lines & Kleinschmidt, 2014
WHO guidance for countries on combining indoor residual spraying and long-lasting insecticidal nets
March 2014

http://www.who.int/malaria/mpac/background-combining-irs-llins-mar2014.pdf?ua=1
WHO guidance: Summary

1. In settings of high coverage with LLINs and where LLINs remain effective, IRS may have limited utility in reducing malaria morbidity and mortality. However, IRS may be implemented with LLINs as part of an insecticide resistance management strategy.1

2. If LLINs and IRS are to be deployed together in the same geographical location, the IRS should use non-pyrethroid insecticides.

3. Malaria control and elimination programmes should prioritize delivering either LLINs or IRS at high coverage and to a high standard rather than introducing the second intervention as a means of compensating for deficiencies in the implementation of the first.

4. Evidence is needed to determine the effectiveness of combining IRS and LLIN in malaria transmission foci, including in low transmission settings. Evidence is also needed from different eco-epidemiological settings outside of Africa.

5. Countries that use both interventions should undertake an evaluation of the effectiveness of combining versus either LLINs or IRS alone.