Minutes of the 2nd Larval Source Management Work Stream Meeting

9.00am-12.00pm, Tuesday 6th December 2011
Marriott Downtown, Philadelphia, PA, USA
(Side Meeting on ASTMH 60th Annual Meeting)

Work stream leader: Steve Lindsay, LSHTM
Rapporteur: Lucy Tusting, LSHTM

Participants: 29

1. **Summary of meeting**
   - The following presentations were made:
     1. Historical use of LSM – Gerry Killeen (IHI)
     2. Cochrane Review of LSM – Julie Thwing (CDC/PMI)
     3. LSM as part of malaria control programs today – Charles Mbogo (KEMRI)

   - The recent draft WHO position statement on larviciding was presented by Michael Macdonald (USAID).

   - Steve Lindsay (LSHTM) and Michael Macdonald led a group discussion of the position statement. The general consensus was that the statement does not fairly reflect existing evidence for the efficacy and cost-effectiveness of LSM and that a revised position statement should therefore be drafted and circulated for further review.

2. **Introductions**
The meeting began at 9.00am and Steve Lindsay (LSHTM) welcomed all participants.

3. **Presentations**

**HISTORICAL USE OF LSM – Gerry Killeen (Ifakara Health Institute (IHI), Tanzania)**
Gerry Killeen gave an overview of the historical successes of LSM in Brazil and Egypt where *Anopheles gambiae* was eliminated by Soper and his team in the 1930s and 40s, using a vertical program of habitat modification and larviciding with Paris Green. He showed photographs to demonstrate the similarities between breeding sites in Brazil and Africa. He described how LSM was successfully used for malaria control in combination with other interventions in the Zambian Copper Belt during the 1930s, through swamp drainage and clearance of vegetation from streams along the Luanshaya River valley. He highlighted that today, such ‘top-down’ programs are inappropriate and that community involvement is necessary. He described how LSM is successfully led today by the community in Malindi,
Kenya. He discussed malaria control using LSM in port-independence Tanzania and the use of LSM today in several wards of Dar-es-Salaam which has been associated with a reduction in prevalence of parasitaemia and density of adult An. gambiae. He discussed unpublished work by Chaki et al which describes how the Dar-es-Salaam urban malaria control program evolved from a local program with local money and little national support, to an institutionalised program that is almost entirely funded by the Tanzanian Ministry of Health and Social Welfare. This demonstrates how sustainable systems can be built.

**Steve Lindsay:** is it appropriate to aim for general mosquito abatement rather than just LSM for malaria control?

**Gerry Killeen:** general abatement is likely to divert focus away from malaria vectors, which are less easy to target than some other mosquito species.

**COCHRANE REVIEW OF LSM FOR MALARIA CONTROL – Julie Thwing (CDC)**

Julie Thwing (CDC/PMI) summarised progress to date and presented preliminary results. The review collaborators are Rob Newman (WHO), John Gimnig (CDC), Julie Thwing (CDC), Steve Lindsay (LSHTM), Ulrike Fillinger (LSHTM), Lucy Tusting (LSHTM), Kimberly Bonner (CDC) and Christian Bottomley (LSHTM) and the objective is to compare mosquito larval source management (excluding biological control with fish) for malaria control with no larval source management, applied either alone or in combination with other malaria control interventions. To date, 2255 abstracts have been identified through an electronic search and 587 through hand search. Of these, 344 abstracts were selected for further review from the electronic search and 181 from the hand search. In total, 526 unique studies have been identified and assessed for eligibility and 14 studies included in the final analysis. Preliminary analysis indicates a significant percent reduction in prevalence of both parasitaemia and splenomegaly and in incidence of clinical malaria in the majority of studies included with these outcomes. The next steps are to update the search to capture 2011 publications, finalise the data abstraction and analysis, submit a draft review, produce a GRADE summary of findings and submit a final version for review and publication.

**Michael Macdonald:** LSM may not fit into the existing Cochrane methodology but this does not mean it should be dismissed.

**Steve Lindsay:** it is important to have an overall ‘take home message’ to avoid the conclusions of the review being lost.

**Gerry Killeen:** the IRS and LSM reviews are likely to have similar conclusions and weight of evidence, yet the difference between the interventions is that IRS can be rolled out everywhere whereas LSM is not a one-size-fits-all intervention and therefore is less attractive.

**Thomas Burkot** (CDC) (author of the Cochrane Review of larvivorous fish for malaria control): the Cochrane group may need to review its methodology, since it is not suited to addressing certain questions. It has been difficult to incorporate the huge volume of historical literature into the larvivorous fish review.
Gerry Killeen: perhaps the issue is that we do not yet have the required refined LSM strategies to roll out.

Michael Macdonald: there is a need for more skills-based products.

**LSM TODAY: CASE STUDIES FROM AFRICA – Charles Mbogo (KEMRI)**

Charles Mbogo gave three examples of current LSM programmes in Dar-es-Salaam, Tanzania, Malindi and Nyabondo, Kenya and Zambia. In Dar-es-Salaam, a large-scale, community-based but vertically managed operational program conducts weekly application of Bti over an area of 55 km\(^2\) and covering a target population of 612,000 people. There has been a significant reduction in malaria prevalence, vector density and abundance between 2005 and 2010. In Malindi, Kenya, community-led integrated vector management is conducted over an area of 32km\(^2\), with monitoring of clinical malaria at health facilities, entomological monitoring, and LSM through regular application of Bti/Bs and environmental management. This has been associated with a 65% reduction in An. gambiae indoor resting densities (2006-2009) and a decline in incidence of malaria cases in 0-5 year olds. In Zambia a feasibility assessment for integrating larviciding into the malaria control programme was conducted in 2008, LSM was launched in 2009 and scaled up to 15 districts in 2010 to complement ITNs and IRS. Here, LSM involves draining mosquito breeding habitats and larviciding using temephos and routine entomological and epidemiological surveillance including insecticide resistance are conducted. A concurrent decline in malaria incidence has been observed at the Konkola copper mines, 1999-2010. Lastly, it was described how the Economic Commission of West African States (ECOWAS) has launched a biolarvicide campaign which aims to eliminate malaria in the region by 2015. The campaign is focusing on strengthening malaria vector control in the region through the use of biolarvicides supplied by the Cuban company Labiofam. Labiofam is currently conducting LSM in Ghana, Angola, Nigeria, Tanzania and Zambia among other countries. It was concluded that LSM is being used as part of IVM in many countries at present and is effective with active community participation and good program and organization management. There is a need for impact evaluations of LSM programs in different epidemiological settings in Africa.

Ngon Chantha (Zambia): LSM was introduced into Zambia in 2005 and was scaled up from three to eight districts. It has been difficult for different districts to generate their own resources to sustain LSM and in the last year, the government has contracted Labiofam to conduct LSM, which has been extended to nearly twenty districts. ‘The manner in which LSM has been conducted leaves much to be desired’, with inconsistent monitoring and an unwillingness to involve the Ministry of Health. This project has now been curtailed.

Chioma Amajoh (NMCP, Nigeria):

1. Labiofam is not conducting LSM as widely as believed, but this will change if new partners are not proactive in Africa.
2. Guidelines and protocols for LSM are necessary.

Gerry Killeen: there is potential for technology transfer and local manufacture of larvicides.
Steve Lindsay: the WHOPES website currently lists different types of larvicide but has not tested specific products, unlike the ITN section which recommends specific brands.

Michael Macdonald: the quality of products does need to be examined. This is a separate issue to the WHO position statement.

4. WHO position statement on larviciding

Jo Lines (LSHTM/RBM) was absent due to illness therefore Michael Macdonald presented the WHO position statement on his behalf. The statement relates to larviciding only.

Reasons given for why a statement is necessary now were as follows: numerous African countries have started, or are planning, major new larviciding programmes, however the larviciding products have not been tested by WHOPES, this initiative is being driven largely by a single Cuban company, in many cases initial recommendation for LSM appears to come from head of state level and this has led to major investment using national (not donor) resources. Lastly, LSM has ‘not passed through the usual process of peer-review and scrutiny’.

The arguments laid out in favour of LSM included 1) the inadequacies of current anti-adult measures (IRS and ITNs) due to insecticide resistance and outdoor biting, 2) the need for an ‘area-wide approach’, 3) cost-effectiveness in some circumstances and 4) it is a ‘failsafe’, i.e. ‘overall control is less sensitive to variations in the effectiveness of larviciding’. Limiting factors that constrain the use of larval control methods were described as follows: 1) it is difficult to locate and treat weekly ≈100% of the breeding sites within the vector flight range, 2) An. gambiae breeding sites are numerous, scattered and a shifting target, 3) a large area must be sprayed (i.e. in order to protect 1 sq km, must prevent breeding over 10 sq km), 4) there is a need for local adaptation and local entomological skills and 5) there are doubts over the cost-effectiveness of LSM i.e. ‘because of diminishing returns, if an intervention is not cost-effective as a primary intervention, it is unlikely to be so as a supplementary’.

The rationale behind the conclusions of the position statement was described. It was firstly stated that anti-adult methods of malaria vector control (IRS and ITNs) are advantageous, due to 1) their amplified effect on transmission (i.e. the Ross-Macdonald model suggested that reducing the biting rate and survival rate has a disproportionate effect on transmission), 2) the long duration of their residual efficacy and 3) their standardised methods. The distinction between urban areas (where houses, which are targets for ITNs and IRS, predominate and breeding sites are few and easy to locate) and rural areas (where breeding sites predominate and houses are few and easy to find) was made. The contrast was made between the era of malaria control pre-DDT, when detailed knowledge of larval ecology was required in conjunction with highly disciplined organization and rigorous enforcement and supervision, and the post-DDT era in which it ‘became possible, for the first time, to deliver effective malaria prevention to large rural populations in remote areas’. IRS requires ‘standard technology that is more or less effective everywhere’.

The position statement makes the following recommendations:
The position statement makes the following conclusions:

1. Larval control is likely to be cost-effective only in situations where breeding sites are particularly few, fixed and easily identifiable. In many parts of the world, including sub-Saharan Africa, such conditions are common in only two circumstances:
   - Urbanised areas – the centres of big towns
   - Desert or extremely arid areas. Note that in some dry areas, larval control may be effective only in the dry season, and not in the wet season when transmission is most intense; this is an important limitation on its overall usefulness.
2. Additional environmental factors that make anti-larval measures more likely to be feasible and cost-effective include:
   - A short transmission season
   - Cool temperatures extending the duration of the immature stages
   - Breeding sites that are man-made and homogenous, so that numerous sites can be dealt with by a single preventive intervention
3. In some circumstances larval control may be feasible with great investment but not cost-effective:
   - If specialised entomological expertise and abundant resources for field operations are available
   - If the area is for example of special economic importance and has high population density. However:
     - In areas that lack the enabling features listed above, including most rural non-desert areas of Africa, IRS (indoor-residual spraying) and LLINs will normally be substantially more cost-effective than anti-larval measures. Persisting with larval control in these circumstances will often result in an inefficient and potentially wasteful use of resources.

5. Discussion of WHO position statement on larviciding

Steve Lindsay:

1. The statement implies that complete coverage of all breeding sites is necessary however this is not always true.
2. The Ross-MacDonald model helped justify the Global Malaria Eradication program however a proportional reduction in mosquito density has been shown to be associated with a proportional reduction in prevalence of infection, for example Matt Kirby’s trial of house screening in The Gambia.
3. WHO supports integrated vector management, and since insecticide resistance has emerged and will undermine ITNs and IRS, a broader perspective is necessary. This might include LSM.

4. The position statement states that an advantage of LSM is that it is a ‘failsafe’ intervention, yet this statement is not correct since no intervention is a failsafe. Malaria will increase whenever an intervention is removed.

5. The argument that ITNs and IRS are more cost-effective than LSM is not supported by any evidence. A recently published analysis by Worrall and Fillinger indicates that LSM is as cost-effective as ITNs and IRS.

6. The WHO statement does not take into account the statement produced by the 1st LSM meeting in February 2011.

7. It appears that the WHO statement has been drafted very conservatively with a view to expanding LSM across Africa if it proves effective on a small scale.

Gerry Killeen:
1. The statement is ‘not as overwhelmingly unreasonable as expected.’
2. Decades of learning and operational research are necessary for LSM and rigorous independent evaluation of impact and management processes are also essential.
3. The cost-effectiveness criticism of LSM is weak since the cost-effectiveness of any intervention declines with a reduction in malaria, therefore a supplementary intervention will always be less cost-effective than the first intervention.
4. The position statement fails to recognise the potential utility of LSM in many countries which have high population densities at high altitude, for example Ethiopia.
5. There are areas where LSM is definitely appropriate (e.g. urban areas), areas where LSM is definitely not appropriate (e.g. Gambia River floodplains) and many ‘grey’ areas where it is unclear whether LSM is appropriate.

These points were then summarised as follows:
1. Impact and process evaluation of LSM are crucial.
2. Refinement of stratification of areas appropriate for LSM is required.

Rose Peter (Arysta Life Sciences):
1. The WHO statement should contain special consideration for countries using LSM in elimination.
2. Niger has not been mentioned yet LSM is being used there alongside IRS and it may be helpful to understand why this strategy has been adopted.

Michael Macdonald: a special note should be made on LSM for elimination and pre-elimination.

Jennifer Stevenson (LSHTM):
1. In the highlands of Western Kenya there are clearly identifiable transmission hotspots where LSM would be appropriate.
2. In this region, the majority of biting now occurs outdoors before 9.00pm. LSM could help reduce this.
3. A new intervention trial is being initiated next year in this region, with ITNs, focal screening and treatment and LSM in transmission hotspots. Communities will conduct larviciding which should minimise its costs.

**Willem Takken** (University of Wageningen):
1. Since the WHO position statement is being directed at ministries of health who are responsible for directing countries’ resources, the statement ‘LSM has a limited role in vector control’ is ‘offensive’.
2. At a current study site in Western Kenya, 90% breeding are man made so are easy to identify.

**Michael Macdonald**: the statement is directed at ministers of health who may have limited experience of LSM and Labiofam, however that the statement perhaps reads more strongly than it should.

**Pete DeChant** (Valent Biosciences Corporation): the statement ‘LSM has a limited role in vector control’ could be altered to ‘LSM has a supplementary role in malaria control.’

**Silas Majambere** (IHI):
1. The original draft WHO position statement is largely inaccurate.
2. The statement should not imply that malaria control program managers must choose one intervention over another, but should emphasise that a combination of vector control interventions is required.
3. The statement implies that LSM is not cost-effective, however it should be remembered that no intervention is 100% effective.
4. LSM is already being conducted in Africa (as was apparent at the recent WHO Africa Region Technical Consultation on Malaria Vector Control, Brazzaville, Congo, 26-28th October 2011) and this will continue, therefore it is necessary to help implement LSM correctly rather than dissuade program managers from using it altogether.

**Gerry Killeen**:
1. The WHO statement will politicise LSM and create a division between WHO and African ministries of health.
2. The WHO statement is attempting to advise governments on the best way to allocate resources. Its negative stance will therefore make it difficult for technical experts to engage with governments.

**Michael Macdonald**: technicians will not take the WHO statement seriously unless it is evidence-based and supported by references.

**Willam Takken**: in 2008 WHO adopted integrated vector management, yet this statement appears to contradict this.

**Chioma Amajoh**:
1. Caution is required since no method is superior to others. Rather, the effectiveness of an intervention depends on the manner in which it is implemented.

2. At the recent Technical Consultation on Malaria Vector Control, Brazzaville, many objections were raised to the WHO position statement however the revised version presented today appears not to take these into account.

3. It is the governments of West African countries which are driving the introduction of LSM and Labiofam is simply facilitating this.

4. Technical documents are required so that LSM can be implemented correctly.

These points were then summarised by Michael MacDonald as follows:

   1. The WHO position statement needs to be a more technically based document.

**Steve Lindsay:**

   1. The process by which the statement has been drafted has not taken into account 1) the statement produced at the 1st LSM meeting, February 2011, 2) comments made at the recent Brazzaville meeting, 3) comments made by numerous parties after circulation of the first draft by email. The statement has also been drafted by one or two individuals only.
   2. Instead, the statement should 1) incorporate conclusions of the Cochrane Review when it is published, 2) take into account the recent paper by Fillinger and Worrall on cost-effectiveness.
   3. WHO is ‘stormtrooping through opinion and evidence.’
   4. The statement should ideally be reviewed by a WHO guidelines committee.

**Graham White:**

   1. LSHTM would be a good location to hold a meeting to refine the statement.
   2. The WHO Global Malaria Program (GMP) has a history of ‘overstepping the line’. ITNs were unpopular when first proposed in the 1980s and the idea was quelled for a decade by GMP.

**Julie Thwing:**

   1. From the PMI perspective, it is evident that WHO may be trying to prevent a certain approach, i.e. ‘throwing millions’ at the problem.
   2. LSM was historically used because it was easy and cheap. Today, LLINs and IRS are being increasingly undermined by outdoor biting and insecticide resistance, and the argument that LLINs and IRS are more cost-effectiveness is questionable once more expensive chemicals need to be used for these.
   3. The statement, ‘LSM has a limited role in malaria control’ contradicts previous WHO statements such as GMAP (2008).
   4. Malaria control is becoming increasingly focal and LSM is amenable to this.
   5. LSM should not be applied everywhere without thought.
   6. LSM requires careful monitoring.

**Gerry Killeen:** The fundamental principal of integrated vector management (IVM) is evidence-based decision making, and one component of this is aimed to help program managers
monitor and evaluate their own progress. This statement will slow down progress. The statement could be improved by including statements on evaluation.

**Steve Lindsay:** ‘no intervention without evaluation.’

**Michael Macdonald:** It will be necessary for us all to help craft a more robust and useful document, which emphasises the need for 1) evidence-based decision making (IVM), 2) good management and 3) quality control

**Gerry Killeen:** quality control of processes (by those independent from those implementing LSM) is crucial in addition to the quality control of products.

**Graham White:** The next meeting of the Work Stream is planned for early February in Geneva and it would be good to draft a new statement for discussion then.

**Steve Lindsay:** Moving forwards, we will crystallise this discussion and circulate a revised statement for review, which takes into account points raised at this meeting and which has more structure rather than being a series of bullet points.

**Michael Macdonald:** Drafting the statement is a large task for one individual (i.e Dr. Abraham Mnzava of the GMP) therefore the Work Stream will need to help.

**Robert Farlow:** If the urgency for releasing a statement is to address the actions of Labiofam, then the solution is not to produce a consensus statement but to advise countries specifically on this issue.

**Michael Macdonald:** program managers are under pressure from those higher up in government to use Labiofam.

**Steve Lindsay:** WHOPES testing is the most appropriate way to address the issue of Labiofam.

**Johnson Ouma (Vector Health):** The Labiofam issue is one of process rather than testing.

**Graham White:**
1. The Labiofam story is not good and it should be emphasised that LSM will play a supplementary role only.
2. The IVM guidelines have not been released as an official document yet but will cover LSM.

**6. Close of meeting**
The meeting was closed by Steve Lindsay who thanked those present and concluded that comments raised will be condensed into an evolved position statement which will be circulated for review.

**7. Dates of next meeting**

Minutes of the 2nd Larval Source Management Work Stream Meeting 9/10
8. Agenda

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<td>Welcome and introductions</td>
<td>Steve Lindsay (LSHTM, UK)</td>
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<td>9.15 - 9.35</td>
<td>Historical success of LSM for malaria control</td>
<td>Gerry Killen (IHI, Tanzania)</td>
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<td>9.35 - 9.55</td>
<td>Cochrane Review of LSM for malaria control</td>
<td>Julie Thwing (CDC, USA)</td>
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<td>9.55 - 10.30</td>
<td>Break</td>
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<td>10.30 - 10.50</td>
<td>Reports on LSM today in individual countries</td>
<td>Charles Mbogo (KEMRI, Kenya)</td>
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<td>10.50 - 11.10</td>
<td>WHO position statement</td>
<td>Michael Macdonald (USAID/RBM)</td>
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<td>11.10 – 12.00</td>
<td>Open discussion and close of meeting</td>
<td>Led by Steve Lindsay (LSHTM)</td>
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9. List of participants

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