Interim Position Statement

The role of larviciding for malaria control in sub-Saharan Africa

World Health Organization

Global Malaria Programme

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Executive Summary

A range of anti-larval methods is available for control of malaria vectors; this paper focuses on larviciding, which is the regular application of chemical and biological insecticides to breeding sites. This is an interim position statement which presents current recommendations about larviciding for the purposes of malaria vector control and within the context of integrated vector management (IVM) in sub-Saharan Africa. The statement does not address the use of larviciding to control vector species of other mosquito-borne diseases nor in other regions of the world where the context is different.

a) Larviciding has a specific and limited role in malaria vector control.

b) The number of unbiased studies on the efficacy or effectiveness of larviciding in Africa is very limited, and makes it difficult to draw generalized conclusions.

c) In order to be effective, larviciding must be specially adapted to each locality, and must be carried out thoroughly and selectively (not all water bodies are important vector breeding sites), often over a large area.

d) In general, larviciding should be considered for malaria control (with or without other interventions) only in areas where the breeding sites are few, fixed and findable.

e) In all rural and most moderately urbanised areas with active malaria transmission, adult mosquito control with insecticide treated nets (ITNs) (including long-lasting insecticidal nets, LLINs) and indoor residual spraying (IRS) are currently considered the most cost-effective interventions, as long as WHO recommendations on insecticide resistance management are followed.

f) Measures which reduce vector longevity, such as ITNs and IRS, have greater potential impact than measures which reduce only vector density, such as larviciding.

g) In most endemic settings, the appropriate way to use larviciding is as a supplement to ITNs or IRS; only in a very few specific circumstances with low transmission will it be appropriate to deploy larviciding alone and in the absence of measures against adult mosquitoes.

h) In sub-Saharan Africa, larviciding measures may be effective as the leading method of vector control in urban areas; however, more good quality evidence is needed to support this view.

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1 A fixed breeding site need not be permanent, but could be a pool of relatively long-standing duration that persists during or beyond the rainy season.
i) The consensus among vector control specialists, based on currently available evidence, is that in most situations, larviciding with universal coverage across large areas and populations is unlikely to be feasible.

j) This information needs to be brought to the attention of policy decision makers in WHO member states to ensure that larviciding is only implemented where it is appropriate, and that vector control resources are used where they are expected to be cost-effective.

k) As with ITNs and IRS, sustained entomological monitoring is needed to guide decisions about vector control - including larviciding. Strengthening capacity in entomological skills is essential to ensure that control programmes at the national and local level are able to make decisions on where larval control is and is not appropriate.

l) Commercial larviciding products can be of variable quality, and quality control is an important issue. The website of the WHO Pesticide Evaluation Scheme (WHOPES) describes standard methods for testing larvicides and gives a list of recommended larviciding products\(^3\), which have been found to be safe, of good quality, and reliably effective when properly applied. Only WHOPES recommended products should be used for larviciding.

**Interim Recommendations**

1) In general, anti-larval measures are likely to be cost-effective for malaria control ONLY in settings where the vector breeding sites are:
   a) **few**,
   b) **fixed** and
   c) **findable**.

2) In sub-Saharan Africa:-
   a) Larviciding measures should normally be used only as a supplement to the core interventions (ITNs or IRS); larviciding should never be seen as a substitute for ITNs or IRS in areas with significant malaria risk.
   b) Larviciding is most likely to be cost-effective in **urban** areas, because the conditions defined above are more likely to be present.
   c) In rural settings, larviciding is not recommended unless there are particular circumstances limiting the breeding sites, as well as evidence confirming that such measures can reduce the malaria incidence rate in the local setting.

3) Additional environmental factors that make larviciding more likely to be feasible and cost-effective include:

\(^3\) [http://www.who.int/whopes/Mosquito_Larvicides_sep_2011.pdf](http://www.who.int/whopes/Mosquito_Larvicides_sep_2011.pdf)
a) a short transmission season;
b) cool temperatures extending the duration of the immature stages;
c) breeding sites that are man-made and homogeneous, so that numerous sites can be dealt with by a single preventive intervention.

4) Further evidence is needed of the value of larviciding as a routine and large-scale operation in both urban and rural areas; this evidence should examine not only questions of feasibility and effectiveness, but also issues of management, economics, environmental and health impacts and cost-effectiveness as a supplement.
1. Introduction

There is renewed interest in attacks on the breeding sites of malaria vector mosquitoes (‘larval source management’, LSM) as a means of malaria control\(^4,5,6\). There is a range of possible LSM interventions, ranging from permanent environmental engineering projects to larviciding. The latter involves the regular application of chemical or biological agents to kill mosquito larvae in their aquatic habitats. Thus the objective of LSM is to either kill the mosquito larvae or create a situation which is unfavourable for mosquito breeding.

Several African countries are currently planning to expand larviciding activities\(^7\). Effective larviciding for malaria control requires precise knowledge of the local breeding sites as well as intensive, widespread and sustained field operations. An important question is therefore whether or not malaria control programmes have the necessary specialised local expertise and operational resources. For these reasons, WHO has been asked by a range of partners to clarify its recommendations concerning the role of larviciding as a means of malaria control. Since larviciding must compete for public resources with other interventions that are proven and life-saving, it is important that the decision-makers have access to independent and evidence-based guidance as to where and when such methods should and should not be used. Where there are several potentially effective approaches there is a need to consider the level of priority of the alternatives.

Most vector control experts agree that there are some specific circumstances where larviciding programmes can be cost-effective and useful for malaria control, and many other circumstances where such efforts are unlikely to be cost-effective\(^8\). For malaria vector control, the key question is how national programmes can identify those specific situations where larviciding is likely to be useful and cost-effective.

This question is part of the broader task of deciding which vector control intervention (or combination of interventions) is likely to be most cost-effective in a given setting, and should therefore be deployed for malaria control purposes by a public health programme. The principles of Integrated Vector Management\(^9\) were developed to provide rational and evidence-based guidance to this task.

\(^7\) Notably, these programmes are mostly using national rather than donor resources.
The relative cost-effectiveness of alternative interventions in a given setting depends not only on the local environment, but also on the specific biology of the local vector species. Each sub-region of the malarious world has its own range of vector *Anopheles* species, and each species has its own characteristic breeding site preferences. Thus, a universal set of rules covering every vector and every possible situation would be vast and complex.

Hence, this position statement does not explain the operational procedures of larviciding; instead it focuses on the general principles of where and when larviciding should be used for malaria control. It includes some observations about anti-larval measures in general, but the specific recommendations are focused on the role of larviciding, with special reference to Africa. Other forms of LSM, including the potential of community-based larval source reduction initiatives, as well as larviciding outside the context of sub-Saharan African will be considered in future WHO documents.
2. Key features of larviciding compared to other methods

2.1 The potential advantages of larviciding

In most settings, insecticide treated nets (ITNs) - which include long-lasting insecticidal nets (LLINs) - and indoor residual spraying (IRS) are the most powerful, reliable and practicable tools for malaria vector control; however these two interventions are not perfect, and they cannot serve all vector control purposes in all settings.

For example, it has often been observed in Africa that indoor transmission can be greatly reduced by careful indoor residual spraying (IRS)\(^{10}\), but outdoor transmission may persist and prevent the complete interruption of transmission. However, it is important to note that major African malaria vectors prefer to rest indoors, where they are exposed to insecticides, even if they sometimes bite outdoors. Larviciding has the potential to overcome this problem, because it is expected to affect indoor and outdoor biting vectors equally.

Similarly, larviciding may sometimes have the potential to play a role in insecticide resistance management, although as of yet, there is no direct evidence that such a strategy will work. Of the larvicides that are recommended by the WHO Pesticide Evaluation Scheme (WHOPES), the majority have never been used to kill adult mosquitoes and are unaffected by the resistance mechanisms currently spreading through malaria vector populations in Africa.

Consequently, larviciding can only potentially play important role in those settings where the procedure is feasible and cost-effective.

2.2. Limiting factors that constrain the use of larviciding

The feasibility and cost-effectiveness of anti-larval methods in general is constrained by two features of anopheline biology: the types of water-body in which such mosquitoes breed, and how far they fly.

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\(^{10}\) Kouznetsov RL (1977). Malaria control by application of indoor residual insecticides in tropical Africa and its impact on community health. Tropical Doctor 7, 81-91
For larval control to be effective, one must find and effectively prevent breeding in a very high proportion of the breeding sites located within the vector flight range of the community to be protected. It is normally not hard to kill the larvae in the breeding sites that one knows about: there is a variety of available methods, including environmental management, as well as the use of chemical and biological larvicides. The main challenge is finding an adequate proportion of the sites over a sufficiently large area to reduce adult mosquito densities (and hence transmission) in the target community, despite the constant inward movement of adult mosquitoes from breeding sites outside the intervention area.

2.2.1 Finding the Sites: To be effective, anti-larval measures must be targeted at the most productive breeding sites of the local vector species. This normally requires local studies to identify those sites, since there is great variation not only among species, but also among locations for a given species.

Many important malaria vectors - notably *Anopheles gambiae s.l.* - breed in a wide range of aquatic habitats. These range from small temporary bodies of water to the margins of semi-permanent and permanent streams and ponds. Maintaining complete coverage of the small and temporary sites – including those scattered around the margins of larger water bodies – is important but difficult. This is because the smaller sites are often numerous, scattered and shifting, i.e. they can be new and slightly different locations every week, as old breeding sites dry out or are washed away, and new breeding sites are created elsewhere (see Figure 1).

Because new breeding sites are always appearing, and eggs laid in new sites may reach adulthood in just 7-10 days, it is normally necessary to repeat larviciding operations at weekly intervals, whatever the residual characteristics of the product used. This is not usually the case in places where the majority of the breeding sites are permanent i.e. cement lined pits or brick pits.

A few vector *Anopheles* species tend to exploit breeding sites that are relatively fixed – for example *An. funestus* in swamps and waterlogged grassland in Africa, and *An. sundaicus* in coastal brackish water in Southeast Asia. Some of the best examples of effective malaria control using larval source management have been targeted at such species. For example, environmental engineering interventions that replace

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brackish water lagoons with 100% sea water can permanently prevent the breeding of brackish-water specialist species. Such opportunistic environmental interventions are normally expensive to install but inexpensive to maintain. They must be distinguished from larviciding operations, where a single operational round of treatment may be relatively inexpensive, but must be repeated every week for as long as transmission control is needed. Larviciding operations should therefore not be considered as a more fundamental, more permanent or more environmentally-friendly form of intervention than ITNs or IRS. In any case, each locality needs its own intervention plan, targeting the most productive local sites, and based on local entomological knowledge.

- This need for local adaptation and local entomological skills is a critical limitation on scaling-up of all kinds of larval source management measures, including larviciding.

### 2.2.2 Large Area

*Anopheles* mosquitoes have a long flight range in open country; females are able to fly up to 1-1.5 km. For this reason, breeding must be prevented within a diameter of up to 3 km, or an area of potentially more than 9 km$^2$, in order to protect a small community inside that zone. In larger communities, the whole area of the settlement plus a buffer region between the community and breeding sites must be covered$^{15}$.

- It is a formidable challenge, during the rainy season, to find every potential breeding site throughout such a large area.

In addition, the fact that larval control can only be effective if carried out on a large scale has implications for three aspects of the evaluation of larval control methods:

- **Indicators:** It is not enough to show that larvae are killed or excluded from sites that are known and treated; rather the critical test is to show whether adult mosquito densities (and ideally, malaria incidence) have been reduced in the target community;
- **Trial design:** If larviciding is only effective when performed over a large area, then the minimum area of a replicate unit within a randomised controlled trial (RCT) must be similarly large. This means that larviciding trials must be conducted on a large scale, even by the standards of conventional vector trials$^{16}$;
- **Limited Evidence:** This requirement for scale makes trials expensive, and has been an important constraint on efforts to collect rigorous, unbiased, and conclusive evidence on the effectiveness of larviciding in a wide variety of settings.


$^{16}$ See Majambere et al (2010), above.
2.3 The advantages of anti-adult methods of malaria vector control (IRS and ITNs)

Methods of killing adult mosquitoes with residual insecticides have some critical advantages over anti-larval methods:

2.3.1 Exponential Effect on Transmission: With ITNs and IRS, female mosquitoes suffer a repeated risk of being killed every time they take a human blood meal. This reduces not just the size of the mosquito population, but also its mean lifespan. Transmission of malaria is extremely sensitive to the lifespan of the vector, because the parasite takes at least 10 days to develop inside the mosquito, and this is a long time relative to the life of a tropical mosquito.

Measures that target longevity of the adult vector would theoretically result in far greater reduction in potential transmission than measures that would reduce the number of vectors only\(^1\). Larviciding affects the rate of emergence and hence number of adult vectors, and has virtually no effect on adult longevity. ITN and IRS are generally more powerful methods of malaria vector control, mainly because both can reduce vector longevity and density and, in the case of ITNs (and with some IRS insecticides), human-vector contact as well. They also target mosquitoes associated with biting humans, and therefore most likely to become infective. They are capable of producing sustained reductions in potential transmission even when actual coverage is only moderately good. Transmission can be reduced to an extremely low level if a large proportion of the infected vectors are killed before the parasite attains an infective stage within the mosquito vector. By contrast, anti-larval methods can never produce more than a directly proportional effect on transmission. If density of adult mosquitoes is reduced by 50% by larviciding, the best that can be hoped for under ideal conditions is reduction of the transmission potential by 50%. However, reducing the life span of a normally long-living vector in tropical conditions by 50% can result in reduction of the transmission potential by 99% or more\(^2\).

Vector longevity is a key factor underlying some major epidemiological patterns in malaria. For example, the fact that *Anopheles gambiae s.l.* and *An. funestus*, the main malaria vector species in Africa, are especially long-lived, compared to their equivalents in other continents, is an important reason why Africa suffers more than 80% of the world’s malaria disease burden. Similarly, the fact that malaria in Southeast Asia is so closely associated with highland forests reflects the fact that one group of human-biting *Anopheles* species in the forest have a particularly long lifespan, while those outside the forest are all relatively short-lived.

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Although the importance of these effects has been recognised by malaria epidemiologists for more than fifty years, they are not well known outside this specialised world. As a result, non-specialist health professionals often assume, wrongly, that larviciding and anti-adult measures should, if carried out with equal care and completeness, have similar effectiveness. This is not true: in fact, coverage with larviciding needs to be much more complete than coverage with ITNs and IRS, in order to have the same effect on malaria transmission. Another claim is that anti-larval measures somehow deal with the root of the problem (“prevention is better than cure”), whereas ITNs and IRS are a short-term measure aimed at the symptoms not the cause. It is true that in some settings, it may be possible to achieve permanent source reduction through environmental interventions and landscape-engineering; history confirms that this kind of “building-out” of malaria can play an important long-term role in consolidating progress towards elimination. However, it is misleading to make such claims about larviciding, the effects of which are even more superficial, temporary and transient than those of ITNs and IRS.

Finally, it may be noted that Anopheles mosquitoes are especially vulnerable to ITNs and IRS because several important vector species tend to rest on indoor walls, and to bite exclusively at night. By contrast, the vectors of many other mosquito-borne diseases (e.g. dengue and other arboviruses) tend to rest on other (non-sprayed) indoor surfaces, and/or to be day-biting. As a result, these other mosquitoes tend to be less vulnerable to ITNs and IRS, and anti-larval methods are the primary means of vector control for these diseases. Similarly, it is worth noting that the main aim of mosquito control programmes in northern Europe and the USA is to control nuisance-biting, not disease transmission, and this is one important reason for their use of larviciding. Thus, the fact that larviciding is used for mosquito control in Europe and North America does not imply that it is the intervention of choice for malaria control in the tropics.

**2.3.2. Long Duration of Residual Efficacy:** ITNs and IRS are effective for months or years. By contrast, in most situations, larvicide treatments need to be re-applied every week. There are some larvicide formulations that have a much longer duration of residual activity in favourable conditions, but in practice, new breeding sites are always appearing, and the water in more permanent sites is constantly flushed out and replaced; for this reason the maximum interval between operational rounds is normally one week.

**2.3.3 Standardised Methods:** Both ITNs and IRS use standardised methods: they are executed in more or less the same way, and are more or less effective against vectors with a wide range of behaviours. It is this technological standardisation that has allowed them to be delivered in a very wide range of circumstances by teams with no entomological knowledge or skills, and still be effective. This in turn has allowed massive scaling-up. We now accept that programmes using these methods can routinely deliver effective protection against malaria to tens or even hundreds of millions
of people. This was unthinkable before the advent of IRS. There remains no evidence that larviciding can be delivered effectively at this scale in Africa, despite the fact that larviciding is useful in specific settings and at a local scale.

2.4 Larviciding as a supplementary measure

A further difference between larviciding and ITNs/IRS is that use of the core interventions of ITNs/IRS is supported by an extensive body of evidence particularly in Sub Saharan Africa. The evidence shows that ITNs and IRS produce substantial reductions in the burden of malaria, and do so consistently across a very wide range of epidemiological settings. With larviciding, the evidence is much less extensive. There is not sufficient evidence to support the use of larviciding as a stand-alone intervention, instead of the core interventions, in areas where there is a significant risk of malaria for a substantial fraction of the population. Therefore, in endemic areas, resources intended for core malaria control interventions should not be used instead for larviciding.

Larviciding may, however, be used as a supplement to these core interventions, depending on the objectives and resources of the programme. As always, larviciding should only be considered in areas where the breeding sites are particularly vulnerable (few, fixed, and findable), and where there is the opportunity to eliminate all or a large proportion of the breeding sites with little effort.

In considering the use of larviciding as a supplementary intervention, in addition to ITNs or IRS, it is important to note the following characteristics of the potential interaction between the interventions:

- The effect of larviciding on malaria transmission is expected to be independent of that of ITNs and IRS, i.e. the effect is expected to be additive, but neither synergistic or antagonistic.
- The cost-effectiveness of combination interventions may be affected by the fact that the incremental benefit of the second intervention is likely to be less than if it had been applied alone. Suppose two interventions act independently, are equally costly and each applied independently reduces transmission by 60%. Thus, the residual transmission is 40% of baseline in the presence of one intervention, and 16% of baseline with both. Thus, the second intervention prevents 60% fewer cases than the first, and in terms of dollars per case prevented, it is 2.5-times less cost-effective, assuming that the cost per person at risk is the same. In reality, there is likely to be overlap in effect between many interventions, so the benefit of the second intervention may be less than given in this example.
- If resources are limited, then the provision of both interventions to some people may be possible only if other people are left with no protection at all. In this
case, the additional risks for the latter must not be forgotten, and must be balanced against the benefits for the former. In general, therefore, a national strategy of "universal coverage with the locally-most-cost-effective single intervention" is normally to be preferred over a strategy of "double protection to some of the at-risk population, but no protection to others equally at-risk".

2.5 Larviciding as a stand-alone measure

At the geographical fringes of malaria, areas with and without local transmission may lie close together. In the locations where transmission is absent most of the time, infected people may arrive frequently from nearby endemic areas, resulting in a constant risk that transmission by local vectors could resume. Thus, some form of vector control may be needed, even though malaria risk is low. In such settings, general coverage with ITNs or IRS is not cost-effective and not justified. In these circumstances, larviciding may be used to consolidate elimination and reduce receptivity, and hence to prevent the re-appearance of malaria outbreaks. This is especially appropriate in settings where hotspots of high transmission risk are known to be associated with breeding sites – for example urban cultivation in the centres of large African cities or irrigated rice in otherwise arid areas. In such situations, larviciding (or other anti-larval measures) targeted at these hotspots may be used as a stand-alone intervention, in order to reduce the risk of resumption of transmission.

3. Lessons from Experience

Having considered the special features of larviciding, vis-à-vis other forms of malaria vector control, we may consider the lessons that may be drawn from experience in the past, including cases where larviciding and other larval control methods were deployed successfully.

As background, it is useful to note a passage from the 2004 meeting of the WHO Study Group on Malaria Vector Control and Personal Protection:

"Before the discovery of DDT, the main approach to controlling anopheline vectors was directed towards the larval stage, which required a detailed knowledge of the bionomics of local vectors. In some cases, a high level of community participation (often enforced by legislation) and a continuity of effort for decades were needed to ensure slow, but often sustainable, progress. Only in projects of very high economical and political value was a highly disciplined organization rigorously enforcing the application of anti-larval measures able to achieve spectacular successes, even in relatively large areas, notably

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the eradication of invading populations of *Anopheles gambiae* s.l. from Brazil and *An. arabiensis* from Egypt or the sanitation of the Pontine Marshes in the Roman Campagna. In other cases, detailed knowledge of species habitats led to methods of environmental manipulation and sustained, cost-effective control, as in parts of Malaysia and Indonesia. In each situation, the solution of a local malaria problem required an in-depth study by a multi-disciplinary team to design a multi-sectoral programme.”

According to statements and reports from the late 1930s (just before the advent of DDT), by the Malaria Committee of the Health Organization of the League of Nations, effective control of malaria was considered to be a realistic and feasible objective only in a limited set of specific situations\(^2\). For most poor rural communities it was regarded as out of reach\(^2\).

An example of what could be achieved in such a suitable situation can be seen in Watson’s account of his work in Zambian copper mines\(^2\). This is best known as a showcase example of effective malaria control using larval control measures including larviciding, in a rural (or semi-urban) African setting in the 1930s. However, it is notable that in 1946, these same mines were among the first to try out the new method of indoor residual spraying (IRS) with DDT, and this innovation was associated with a considerable further reduction in malaria cases.

With the advent of DDT and IRS, effective malaria vector control became possible not only in areas of special economic importance, such as the mines, but also, and for the first time, in ordinary rural communities in remote rural areas. The spraying itself was technically and logistically demanding, but it had two great operational advantages. First, it needed to be repeated only once or twice a year -- whereas in most breeding sites, chemical larviciding needs to be repeated every week during the season. Second, it consisted of a standardised and uniform set of methods, and therefore could be scaled up rapidly to cover very large populations -- whereas anti-larval methods are effective only if carefully targeted to the most productive local breeding sites, a task that requires specialised entomological investigation in each new area.

The advent of IRS did not cause the complete disappearance of all forms of larval control everywhere, but it caused anti-larval interventions to become more restricted, i.e. there was a move towards (a) more permanent forms of environmental modification, and (b) use of larval source management in places where breeding sites are obviously restricted and therefore vulnerable to complete elimination.

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Later, with the development of LLINs, malaria control gained an intervention that was even more standardised, and that was capable of being delivered at even longer intervals. This extended yet further the ability to deliver effective vector control to the most remote areas, without the need for local adaptation or entomological skills.

4. Which settings in Africa are suitable for larviciding?

4.1 Urban Areas  Most vector control experts would agree that larviciding can be effective and useful for malaria control in some urban areas in Africa where malaria transmission exists. It is likely to be worth considering also in densely populated refugee camps and internally displaced person camps. If carefully executed and sustained, such methods may even be adequate as the main vector control intervention in the densely urbanised centres of major cities.

The reason for this urban-rural contrast is simple. The process of urbanisation creates a high density of humans, but reduces the density of African malaria vectors\(^{23}\), which tend to avoid breeding in water that is enclosed in concrete, or in other man-made containers\(^{24}\), or in water with rotting organic matter. The intensity of malaria transmission is therefore much lower in towns than in the surrounding countryside. For this reason, as one moves from the countryside into town, the relative effort needed to deliver either anti-larval or anti-adult interventions is reversed. This is illustrated in Table 1.


\(^{24}\) An exception to this rule can be seen in some arid parts of Sudan, Somalia and Yemen, where there is dry-season breeding of \textit{An. arabiensis} in man-made water-storage tanks… and since these are typically few, fixed, uniform and easy to find, anti-larval interventions in these sites can be effective as a means of malaria control.
Table 1: The urban – rural contrast

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<th>Houses/breeding sites</th>
<th>Urban</th>
<th>Rural</th>
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<td></td>
<td>Cover most of the landscape</td>
<td>Few, Fixed, Findable</td>
</tr>
<tr>
<td>Houses (target for IRS, ITN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breeding Sites (target for LSM)</td>
<td>Few, Fixed, Findable</td>
<td>Cover most of the landscape</td>
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Delivering ITNs or IRS to all the houses in rural areas is likely to be easier than reaching all the breeding sites. By contrast, in urban areas, breeding sites are limited to a few fixed areas in the gaps between the buildings and it becomes easier and cheaper (in terms of cost per square kilometre or per capita) to reach all the breeding sites every week than to deliver nets or IRS to all the houses at much longer intervals. In other words, the relative cost of larviciding, as well as its feasibility, depends on the human population density relative to the density of aquatic habitats.

Although larviciding is conventionally regarded as appropriate for urban centres in Africa, and there have been some encouraging recent studies, the formal evidence for its general effectiveness is nevertheless very limited. In particular, it remains unclear how programme managers, outside of the context of research studies, can easily identify the urbanised conditions where larviciding is likely to work, and draw a clear line between these and the surrounding rural areas where it is inappropriate. In order to fill this evidence gap, further investigation of the effectiveness of larviciding in urban areas would be helpful, through operational research and implementation on a pilot scale that includes rigorous evaluation of the impact on malaria transmission.

Different *Anopheles* species are affected in different ways by urbanisation and other changes in land-use. This description of the African situation also applies broadly to many other settings, but not, it must be stressed, to India and Pakistan, where *Anopheles stephensi* transmits malaria in urban locations. This important malaria vector species has adapted to breeding in a variety of man-made containers, including water-storage tanks of all kinds. The Indian sub-continent is therefore the only region where malaria transmission is often more intense in towns than in the surrounding countryside.

### 4.2 Arid areas

In deserts, there is hardly any surface water during the dry season; the remaining water bodies are few, fixed and well-known. They are therefore vulnerable to attack by a variety of methods. However, the two critical questions are: (a) is there public health value in attacking the few remaining breeding sites at a time of year when there is almost no transmission, and (b) are the same methods still effective in the rainy season, when for a brief period there may be numerous small breeding-sites all over the countryside? In the majority of cases, the answer to these questions is "probably not", and in these cases, anti-larval measures are not likely to be cost-effective. In a few cases, however, breeding sites may be few and fixed more or less throughout the year, or permanent enough to cause significant transmission even in the dry season, and in these cases, larval control may be worth trying. For example, in arid areas with persistent dry season transmission due to vector breeding in man-made water-storage tanks, there are a few cases where anti-larval measures have been shown to be useful in reducing adult mosquito densities and malaria incidence. In some parts of the world, there is a tradition of attacking dry season breeding sites in order to delay or slow down the expansion of the vector population when the next rainy season begins: although this is an attractive idea, it does not seem to be supported by sufficient evidence or consensus of expert opinion.

### 4.3 East African Highlands

Most recently, a series of trials and pilot operations in Africa have brought renewed interest in the potential role of supplemental larviciding in settings where anti-larval measures have not previously been seen as having a role – for example in the East African highlands. This evidence is encouraging, and justifies further operational research to confirm that these findings can be repeated in similar settings elsewhere. However, as already noted, the most critical questions are: whether it is possible to deliver larviciding, with the requisite quality and completeness of cover, on a much larger scale; whether it is cost-effective as an addition to IRS or LLINs; and whether this can be sustained for years. Pilot operations with careful assessment could help to answer these questions. It is not a straightforward task: it will

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29 See Fillinger U and SW Lindsay (2011) above.
require operational routines that are (a) locally adapted to fit local variations in breeding sites, (b) carefully managed and supervised to sustain constant completeness. For now, and until such evidence becomes available, it is not yet possible to recommend adoption of supplemental larviciding measures in highland areas into routine public health programmes.
5. Priority Research Issues

There are many gaps in the evidence about larviciding, but some of the most important are:

- If anti-larval measures are mostly appropriate in urban centres but not in rural areas, where and how should the line be drawn between the two? What criteria can/should be used? Is it useful to think about the "house to breeding site ratio" or the "breeding sites to person ratio", and how such indices could be defined and potentially used?

- How can supplementary larviciding be scaled up to a generalised routine intervention with universal coverage across large areas and populations, while still providing for operational adaption to local variations in breeding sites, and maintaining the necessary completeness of coverage? How can the process of identifying and targeting the most important breeding sites in an area be streamlined and simplified so that it can be done by non-specialised staff?

- In some environments, many of the most productive breeding sites are man-made, and some forms of man-made breeding site are common in many locations, e.g. brick-making, and cultivation of rice, sweet potato, yam, and some salad vegetables. Are there standard methods by which brick makers and farmers can still work efficiently but avoid producing mosquitoes as an unintended and harmful side-product?

- Since there are already plans for large-scale larviciding in some African countries, can these plans be adapted to allow for more rigorous evaluation, for example using a "stepped wedge" design in comparison with other vector control interventions?

- Can larviciding with different classes of insecticide from those used in LLINs/IRS be used as an insecticide resistance management tool?

- What is the potential of treating dry season larval habitats to limit transmission seasons, in areas such as southern Africa?
Figure 1:

Photos: J Lines & V Robert

Caption:

Muddy hoofprints in Muheza, Tanzania. The picture illustrates the shifting nature of typical breeding sites. This site contained at least some water for most of the year but its size and therefore the location of the water margins fluctuated from week to week. On the day this picture was taken, this was a very productive breeding site: each of these hoofprints contained >100 mature larvae and pupae of *Anopheles gambiae* s.l. (see inset). If the weather over the next few days is dry and sunny, then the wet hoofprints that we see now will dry out, but others will presumably appear in the parts of the stream that are now under deeper water. Conversely, if there are several consecutive days of rain, the hoofprints that are now wet-mud will be submerged completely (and much less productive), but other wet hoofprints will appear further back, in the mud that is now dry. Either way, there will be no larvae here, but there will be wet muddy hoofprints somewhere else, newly colonised by a new set of larvae.