World Health Organization

GLOBAL MALARIA PROGRAMME

Control of residual malaria parasite transmission

Guidance note – September 2014

Background

The current core malaria vector control interventions are long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS), with larval source management (LSM) applicable in certain settings where mosquito breeding sites are few, fixed and findable.[1,2,3] Long-lasting insecticidal nets reduce malaria parasite transmission mainly by killing or blocking mosquitoes that attempt to feed upon humans under nets. Indoor residual spraying kills mosquitoes and reduces longevity when they rest on insecticide-sprayed surfaces inside houses or other structures, usually after they have fed on occupants.

The effectiveness of these interventions relies on a number of factors including susceptibility of mosquitoes to the insecticides used, adequate coverage rates, quality and timely implementation, and user acceptance or compliance. While factors that can limit the effectiveness of existing interventions are extremely important and must be addressed, even full implementation of core interventions would not halt malaria parasite transmission across all settings.

Indeed, evidence from a variety of settings over the last half century indicates that *residual malaria parasite transmission* occurs even with good access to and usage of LLINs or well-implemented IRS,[4,5,6,7] as well as in situations where LLIN use or IRS are not practical. A combination of human and vector behaviours are responsible for this transmission, for example when people reside in or visit forest areas or do not sleep in protected houses[8,9] or when local mosquito vector species exhibit one or more behaviours that allow them to avoid the core interventions.

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[1] World Health Organization (2012). *Larval source management – a supplementary measure for malaria vector control. An operational manual*. Geneva, Switzerland.

[2] World Health Organization (2013). *WHO recommendations for achieving universal coverage with long-lasting insecticidal nets in malaria control*. Geneva, Switzerland.

[3] World Health Organization (2014). *WHO guidance for countries on combining indoor residual spraying and long-lasting insecticidal nets*. Geneva, Switzerland.

[4] World Health Organization (1980). *The Garki Project: research on the epidemiology and control of malaria in Sudan Savanna of West Africa by L. Molineaux and G. Gramiccia*. Geneva, Switzerland.

[5] Govella et al. (2013) Entomological surveillance of behavioural resilience and resistance in residual malaria vector populations. *Mal J*, 12: 124

[6] Durnez and Coosemans (2014) Residual transmission of malaria: an old issue for new approaches. *In* Manguin, S. (Ed.). *Anopheles Mosquitoes – New Insights into Malaria Vectors*. ISBN: 978-953-51-1188-7, InTech.

[7] Killeen (2014) Characterizing, controlling and eliminating residual malaria transmission. *Mal J*, In Press.

[8] Monroe et al. (2014) "People will say that I am proud": a qualitative study of barriers to bed net use away from home in four Ugandan districts. *Mal J*, 13: 82.

[9] Bhumiratana et al. (2013) Malaria-associated rubber plantations in Thailand. *Travel Med Infect Dis*, 11(1): 37-50.

WHO/HTM/GMP/MPAC/2014.5

The main vector behaviours that maintain residual transmission are:

1. Behavioural avoidance such as reduced house entry, diversion from contact with indoor treated surfaces or nets, and early exit from houses. Such avoidance often occurs naturally but may also be due to insecticide-induced irritancy, repellency and/or toxicity[4,5,10,11];
2. Feeding upon humans when and where they are not protected. This includes indoors if not under nets, outdoors, and away from protected houses due to occupational, domestic or recreational activities;
3. Feeding upon animals in preference to humans, thereby having reduced contact with indoor treated surfaces or nets; and
4. Resting outdoors away from indoor treated surfaces.

While much of our knowledge on malaria vector biology and behaviour has been derived from small-scale research projects rather than longitudinal routine surveillance, vector species behaviour is known to vary considerably both within and between locations as well as between seasons and years. There is also evidence that changes in behaviour have apparently been selected as a consequence of vector control and environmental change. Numerous vector species have therefore been implicated in residual transmission and important examples include *An*. *arabiensis* in many parts of Africa,[4,7-9] *An*. *dirus* in South-East Asia,[12] and *An. albimanus and An*. *darlingi* in the Americas.[13,14] In many malaria-endemic areas this residual transmission, maintained through a combination of human and vector behaviours, will render malaria elimination extremely difficult in the absence of new vector control interventions.

Need for new tools and strategies to address residual transmission

National malaria control programmes (NMCPs) must prioritize the implementation of current tools whilst improved or novel vector control interventions are under development and going through the validation process. Meanwhile, the focus should be on assessing the following strategies for effectiveness, practicality and affordability:

1. Exclude or deter indoor entry using physical screening barriers or repellents;
2. Following entry, prevent successful indoor feeding and/or resting using exit or other barriers, repellents, or insecticides with no deterrent properties;
3. Prevent successful outdoor feeding by using insecticide-treated clothing or repellents to directly protect people;
4. Reduce adult vector densities or transmission potential by:
    a. outdoor attractants to lure and trap/kill mosquitoes;
    b. topical or systemic insecticides for livestock that kill mosquitoes during or after feeding; or
    c. applying insecticides to natural sugar sources or by introducing insecticidal sugar baits.

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[10] Chareonviriyaphap et al. (2013). Review of insecticide resistance and behavioural avoidance of vectors of human diseases in Thailand. *Parasites and Vectors*, 6: 280.

[11] Coetzee et al. (2013) Malaria in South Africa: 110 years of learning to control the disease. *Sth Africa Med Journal* 103: 10 (Suppl 2).

[12] Trung et al. (2005). Behavioural heterogeneity of *Anopheles* species in ecologically different localities in South East Asia: a challenge for vector control. *Trop Med Int Health*, 10: 251-262.

[13] Campos et al. (2012). Integrated vector management targeting *Anopheles darlingi* populations decrease malaria incidence in an unstable transmission area, in the rural Brazilian Amazon. Mal J, 23(11): 351.

[14] Chareonviriyapha et al. (1997). Pesticide avoidance in *Anopheles albimanus*, a malaria vector in the Americas. J Am Mosq Assoc, 13(2): 171-183.

Some of these strategies are relatively new and are still under development and some need to be adapted and evaluated in different malaria eco-epidemiological and socio-cultural contexts. The evidence base for informed deployment of improved or novel tools, new paradigms or combined usage with existing interventions, is currently limited. There is heavy reliance on small-scale studies or theoretical analyses with mathematical models, and empirical observations are required at large-scale to verify the added value of these interventions. Once the supporting evidence base is available, policy setting mechanisms within WHO will make appropriate recommendations for implementation by national programmes.

Proposed approaches to accelerate the availability and uptake of new tools

The development, optimization, validation and evidence-based deployment of vector control tools to address residual transmission will require the concerted effort of NMCPs and their partners, including industry, research and academia, and WHO. Whilst new tools are under development and in the process of validation, NMCPs should ensure that the core interventions are implemented optimally.

In collaboration with academic or research institutions, NMCPs should continue to generate local evidence on the magnitude of the problem of residual transmission, including information on human and vector behaviour, and intervention effectiveness. A clear understanding of human behaviour regarding the time and place of exposure to mosquito bites is important.[15]

Industry is further encouraged to develop new tools and technologies for targeting vector populations, which are specifically designed to interrupt residual transmission and thereby address the practical limitations of existing interventions. A costing comparison should be undertaken to ascertain the economic feasibility and scalability of candidate tools and approaches. This will allow prioritization of development initiatives and help to identify where further guidance is needed. Such guidance could include standardized protocols that support the appropriate design and implementation of field trials to determine the effectiveness of candidates across different settings. These trials may be coordinated via research consortia, which are more likely to be able to generate the necessary funding to support large-scale multi-country trials. The steps, procedures and evidence required to validate new forms of vector control tools/paradigms and to introduce them to market are outlined in the report of the first meeting of the WHO Vector Control Advisory Group.[16]

National malaria control programmes and partners may consider conducting well-designed pilot trials of promising new vector control tools in order to provide conclusive evidence on their local efficacy and acceptability. Where feasible, the establishment of experimental hut facilities and semi-field systems (cages or biospheres) at one or two representative sentinel sites will enable assessments of the anticipated field efficacy of new interventions alone or in combination. The deployment of new vector control tools may be progressively adapted and expanded based on robust entomological and epidemiological surveillance and monitoring data. For example, local academic and research institutions may provide additional capacity for advanced assessment of key parameters. Such pilot implementation will not only allow optimization of the effectiveness of tools at national level, but will also contribute to the global evidence base required to inform the development or improvement of tools and define the conditions for their implementation.

[15] Moiroux et al. (2014). Human exposure to early morning *Anopheles funestus* biting behaviour and personal protection provided by long-lasting insecticidal nets. *PLoS One*, 9(8): e104967.
[16] http://www.who.int/neglected_diseases/vector_ecology/VCAG_resources/en/

Epidemiological stratification, sociological and demographic information, and entomological surveillance and monitoring data[17] must be used to inform the implementation of existing and new vector control interventions across all settings. Entomological surveillance must include periodic assessment of vector species composition and abundance, time and place of biting and resting, blood meal sources, and insecticide susceptibility status in representative eco-epidemiological settings. Accurate measurement of key vector behaviours may require new or adapted surveillance tools and approaches.

Also essential is the monitoring of coverage, quality and impact of interventions, including durability of LLINs, insecticidal residual efficacy, and user acceptability and compliance. This will help to define the extent and sources of residual transmission, or other factors that compromise effective coverage, so that interventions can be selected and targeted accurately.[18]

National regulatory systems should facilitate rapid registration of new and validated tools to allow timely deployment.[19] This will require close coordination between national regulatory authorities, NMCPs and vector control product manufacturers.

Establishment and maintenance of entomological surveillance and vector control monitoring systems as well as testing of new tools will require enhanced and sustained human and infrastructural capacity as outlined in previous WHO guidance.[20] Technical training and commitment of resources to entomological surveillance at national, provincial and district levels should be a priority. This also provides an opportunity to strengthen and institutionalize national expertise for operational research within NMCPs.

It is essential that global partners, including malaria endemic countries, continue to invest in local malaria research and control initiatives that support the development and field validation of new forms of vector control tools and technologies for controlling residual transmission. The WHO Vector Control Advisory Group will continue to support the evaluation of such tools, technologies and paradigms in order to speed up their availability for deployment. The WHO Pesticide Evaluation Scheme (WHOPES) requires strengthening and support to expand capacity to accommodate these new developments in the area of efficacy and safety for product specifications.

Conclusions

Universal coverage with LLINs or IRS where appropriate, remains the highest priority for investments in malaria vector control. However, there are many settings in which complete interruption of malaria parasite transmission cannot be achieved by these interventions alone, even with high levels of coverage and best practice implementation. There is therefore an urgent need for new WHO-recommended tools, technologies and guidance to address residual transmission of malaria parasites. Robust entomological surveillance, monitoring and operational research are also required to assess the extent and relative contribution of residual transmission to malaria burden across different settings. This information will inform the implementation of novel or improved vector control tools beyond the existing core malaria vector control interventions.

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[17] Note that a malaria entomological surveillance and monitoring manual is currently under development by WHO.

[18] Any shift from universal coverage with the core interventions must be undertaken with caution, be well informed by robust local epidemiological and entomological data, and should consider the inherent transmission potential in the particular setting.

[19] Vontas et al. (2014) Framework for rapid assessment and adoption of new vector control tools. *Trends Parasitol*, In Press.

[20] World Health Organization (2013). *WHO guidance note on capacity building in malaria entomology and vector control*. Geneva, Switzerland.

Main recommendations

1. National malaria control programmes in collaboration with academic or research institutions should generate local evidence on the magnitude of the problem of residual transmission of malaria, including information on human and vector behaviour, and intervention effectiveness.

2. Industry and their partners are encouraged to develop new vector control tools to address residual transmission. Financial, human and infrastructural resources are urgently needed to support development, evaluation and implementation of such tools.

3. National regulatory authorities should ensure that registration processes support the rapid availability to the local market of validated new vector control products.