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Vector control: a cornerstone in the malaria elimination campaign

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Abstract

Over many decades, malaria elimination has been considered to be one of the most ambitious goals of the international community. Vector control is a cornerstone in malaria control, owing to the lack of reliable vaccines, the emergence of drug resistance, and unaffordable potent antimalarials. In the recent past, a few countries have achieved malaria elimination by employing existing front-line vector control interventions and active case management. However, many challenges lie ahead on the long road to meaningful accomplishment, and the following issues must therefore be adequately addressed in malaria-prone settings in order to achieve our target of 100% worldwide malaria elimination and eventual eradication: (i) consistent administration of integrated vector management; (ii) identification of innovative user and environment-friendly alternative technologies and delivery systems; (iii) exploration and development of novel and powerful contextual community-based interventions; and (iv) improvement of the efficiency and efficacy of existing interventions and their combinations, such as vector control, diagnosis, treatment, vaccines, biological control of vectors, environmental management, and surveillance. I strongly believe that we are moving in the right direction, along with partnership-wide support, towards the enviable milestone of malaria elimination by employing vector control as a potential tool.

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> Malaria control should not be a campaign; it should be a policy, a long-term program. It cannot be accomplished or maintained by spasmodic effort. It requires the adoption of a practicable program, the reasonable continuity of which will be sustained for a long term of years
>
> Boyd (1939)

> Malaria defeated the international community many years ago. We cannot allow this to happen again. A single global action plan for malaria control, that enjoys Partnership-wide support, is a strong factor for success.
>
> Margaret Chan, Director-General of the WHO

Global Burden of Malaria

Nearly half of the world's population is at risk from malaria. It is estimated that, in 2009, the number of cases of malaria was 225 million and the number of deaths was 781 000 [1]. Thirty-five countries are responsible for the majority of the total deaths worldwide. The five main contributors (Nigeria, Democratic Republic of Congo, Uganda, Ethiopia, and Tanzania) account for 50% of global deaths and 47% of malaria cases [2] (Fig. 1).

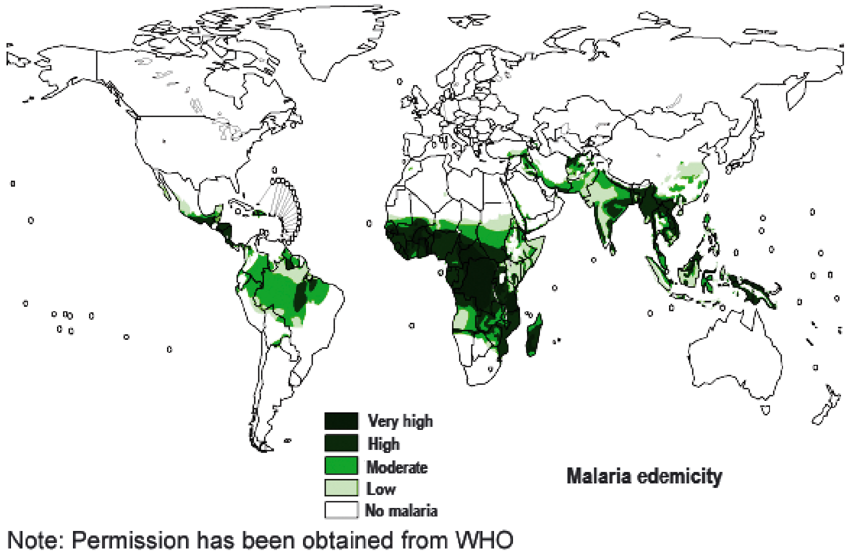

FIG. 1. World malaria map.

History of Malaria Control: Past Experience

To understand malaria today, it is important to acknowledge the history of the disease and previous global efforts made to control and eradicate it. In the mid-nineteenth century, malaria was endemic in most countries and territories of the world, affecting about 90% of the world's population and reaching as far north as the Arctic Circle (Wernsdorfer, Presentation at WHO Informal Consultation on Global Malaria Control and Elimination, January 2008). After successful efforts to reduce malaria with dichlorodiphenyltrichloroethane (DDT), beginning in 1945, in 1955 the 8th World Health Assembly launched the Global Malaria Eradication Campaign for all malarious countries except Madagascar and those of sub-Saharan Africa, using indoor residual spraying (IRS), primarily with DDT, as a vector control tool together with case management [3].

The activities of the Global Malaria Eradication Programme led to the elimination of the disease from countries at the edges of the global malaria distribution, where the intensity of transmission was quite low. In all, 37 of the 143 countries in which malaria was endemic in 1950 were freed from malaria by 1978, with 27 of these being in Europe and the Americas. In many other countries, major gains were made in decreasing the burden of disease and death [3]. However, some of the countries were unsuccessful in interrupting transmission. By 1973, it was concluded that, in certain countries, a 'time-limited eradication program was impracticable' [4], and the emphasis was therefore changed to long-term integrated control programmes.

The priorities of a malaria elimination programme are: (i) to identify and treat malaria patients and all people carrying parasites, including those carrying gametocytes, ensuring that they become non-infectious as early as possible; and (ii) to sustainably reduce human–vector contact and the vectorial capacity of the local *Anopheles* mosquito population, to prevent new infections from occurring [5].

Vector control is defined as measures of any kind directed against a vector of disease and intended to limit its ability to transmit the disease. The current focus on malaria elimination will depend on increasingly effective and affordable vector control interventions.

Methods Against adult Mosquitoes

IRS

IRS is an effective method of vector control, and involves applying a long-lasting insecticide to the inside walls of houses and other structures where people sleep. It is aimed at killing mosquitoes that enter houses when they rest on sprayed surfaces (e.g. walls and ceilings). IRS is widely used in areas of seasonal transmission, including epidemic-prone areas, and increasingly in more malaria-endemic areas. The most common insecticides used are DDT and pyrethroids. IRS is appropriate in epidemiological settings where vectors mainly stay indoors, and in countries where the necessary logistical capabilities can be deployed [6].

In terms of its immediate impact, IRS remains the most powerful vector control intervention for reducing/interrupting malaria transmission. Its use in the last 60 years has played a major role in the elimination of malaria from southern Europe and the Mediterranean, Russia, large parts of Asia and Latin America, and many areas of South Africa. In contrast to the historical impact of IRS, clinical evidence for its efficacy is limited. Interruption of spraying in Latin America, Sao Tome and Madagascar was observed to have a demonstrable detrimental effect on the prevention of malaria transmission [7,8]. Randomized controlled trials have shown that IRS reduces malaria incidence in unstable malaria settings, but is inferior to insecticide-treated nets (ITNs) in this setting [7].

Despite its initial widespread use and contribution to the success of malaria eradication and control efforts, the use of IRS has declined in recent years. This is because of the lack of commitment and financing from governments to sustain these efforts over the long term, concerns about insecticide resistance, and fear of its harmful effects on the environment and human health [8]. IRS is relatively demanding in terms of planning, logistics, infrastructure, the skills required, and the coverage levels that are needed for a successful operation. Reaching areas with no roads, particularly in the rainy season, may be exceedingly difficult.

Ultra-low-volume (ULV) space spraying (fogging)

Space sprays are widely employed for the control of adult mosquito populations worldwide. Space sprays may be applied as thermal fogs, in which kerosene or oil is used as a carrier for insecticides that produce dense fogs of droplets, or as ULV sprays, in which fine droplets of insecticide concentrate are applied. They should be carefully planned, timed, supervised and evaluated by professional staff if they are to be effective. Equipment should be well maintained [9]. ULV space spraying is generally not cost-effective as a means of malaria vector control, as the operational costs are high and residual effects are low. It may, however, be considered for use in exceptional circumstances, such as emergency situations in refugee camps. In this case, if the target mosquito species is exophilic, treatment is applied outdoors wherever the mosquitoes rest. If the vector is endophilic, treatment is applied both indoors and outdoors. Suitable insecticides are applied as cold aerosol sprays or as thermal fogs. Where possible, applications should coincide with the flying times of the local vector [10].

Personal Protection Measures

ITNs

ITNs have become the most widely used form of vector control. ITNs are more powerful than IRS and are usually less demanding logistically; also, their coverage is easier to sustain. Ordinary ITNs need to be retreated every year or so, but this is not the case with long-lasting insecticide nets, which are designed in such a way that the insecticide lasts for as long as the net. ITNs work in two ways: first, they protect the individual user against biting; and second, they can kill some of the mosquitoes that try to bite. Like IRS, the use of ITNs can produce a community-wide reduction in transmission [11]. Deltamethrin is the most abundantly used compound, constituting about 60% of global usage, followed by permethrin (22%) [12].

The effectiveness of ITN interventions in reducing the burden of malaria has been amply demonstrated in a variety of epidemiological settings. ITN use by children in several settings has been shown to be very cost-effective [13]. Randomized controlled trials in Kenya, Ghana, The Gambia and Burkina Faso have demonstrated that wide-scale use of ITNs can reduce all-cause child mortality by approximately one-fifth, saving an average of six lives for every 1000 children aged 1–59 months protected every year [14]. In an area of intense perennial transmission in western Kenya, ITN use reduced episodes of clinical malaria and anaemia in infants by >60% [15], and reduced by nearly one-third the incidence of sick child visits to peripheral health facilities [13].

It has been estimated that adequate coverage of malaria-in-pregnancy control measures, such as the use of insecticide-treated bed-nets and intermittent preventive treatment in pregnancy, may prevent 3–8% of infant deaths [16,17]. In the highly malarious western Kenya, studies indicated that women who were protected by ITNs every night in their first four pregnancies delivered approximately 25% fewer babies who were either small for gestational age or born prematurely than women who were not protected by ITNs. Furthermore, the infant who sleeps under the net with the mother will also have marked benefits: reduced malaria exposure, decreased incidence of anaemia, decreased risk of death, and enhanced development [18]. Where community-level ITN coverage is greater than about 60%, a community effect is seen in which non-users receive similar protection to ITN users [19]. The use of insecticide-treated bed-nets or curtains substantially reduces the burden of malaria [14]; however, we do not know the extent to which these policies might durably reduce malaria morbidity [20]. The major challenges to the implementation of ITN programmes are summarized in Table 1 [21].

Repellents

Chemical repellents are important in protecting people from blood-feeding insects, ticks, mites, and other arthropods, and

TABLE 1. Major challenges in the implementation of insecticide-treated net (ITN) programmes

Problems	Possible solutions/description
Lack of coordination between private and public sectors in the manufacture and distribution of ITNs	Vibrant ITN public–private partnership should be established to promote local manufacture and distribution of nets and insecticides
Lack of affordable (or free) ITNs for the rural poor	This can be remedied by the commitment and support of national programmes and global partners (including Roll Back Malaria (RBM), the US President's Malaria Initiative (PMI), UNICEF, World Bank, Bill & Melinda Gates Foundation, WHO, bilateral and other non-profit human and social development organizations)
Requirement for ITNs to be re-impregnated every 6–12 months to improve their efficiency	This setback can be resolved by the commercialization of long-lasting insecticidal nets
Pyrethroid resistance (observed in Africa)	This must be addressed by discovering and developing new broad-spectrum classes of insecticide with novel modes of action They must be inexpensive, user-friendly, and target-specific A field-based surveillance programme is indispensable for the detection and monitoring of insecticide resistance The households should be subjected to indoor residual spraying (IRS) and other vector control interventions
Due to large coverage of bed nets the malaria vector mosquitoes have changed the biological behavior in particular time of biting, feeding site and blood hosts.	Understanding the biological implications of widespread and long-term ITN use is paramount
Operational problems such as: Equity and access constraints Seasonal variation of ITN use in the community Low rates of net retreatment with insecticides	Initiating social marketing projects to promote ITN usage and creating a favourable environment for scaling up Creating awareness of sustainable malaria prevention through outdoor use of ITNs. Communication on behavioural change to ensure effective use of nets

may therefore also reduce the transmission of arthropod-borne diseases [22]. The majority of commercial repellents are prepared by using chemicals such as allethrin, *N*-*N*-diethyl-*m*-toluamide, dimethyl phthalate (DMP), *N*,*N*-diethyl phenylacetamide, and *N*,*N*-diethyl mendelic acid amide. It has been reported that these chemical repellents are not safe for public use [23,24]. Synthetic repellents have several limitations, including reduced efficacy owing to sweating, expense, and allergic reactions.

Repellent-treated fabrics might obviate some of these limitations. Many species of bloodsucking insects bite predominantly around the ankles and wrists. The *N*-*N*-diethyl-*m*-toluamide-impregnated anklets, wristbands, and shoulder and pocket fabric strips at a concentration of 2 mg/cm^2 provided 5 h of complete protection against mosquito bites, and the reduction in entomological inoculation rate varied between 65.85% and 100% [25]. Strips of cotton fitted around the extremities and treated with a repellent reduce insect/mosquitoe biting significantly [26]. Similarly, DMP-treated wristbands have shown variable degrees of efficacy in repelling different mosquito species. A study has suggested that DMP-treated wristbands are very promising against both day-biting and night-biting mosquitoes [26]. Therefore, they could serve as a potential means of personal protection against insect nuisance and insect-borne disease when and where other kinds of personal protection measures are impossible and impracticable [26]. Impregnation of the repellent into cotton fabric strips is a more reasonable way of minimizing direct skin contact [25].

Plants have been used since ancient times to repel/kill bloodsucking insects, and even today, in many parts of the world, people are using several plant-based products against mosquitoes and other bloodsucking insects [27]. Plant products can be used either as insecticides for killing larvae or adult mosquitoes or as repellents for protection against mosquito bites, depending on the type of activity that they possess. A large number of plant extracts have been reported to have mosquitocidal or repellent activity against mosquito vectors [28]. Repellents of plants origin are currently receiving massive attention, owing to their environmental and user-friendly nature [29].

Various plants have been reported to possess repellent activity against mosquitoes, and *Azadirachta indica*, *Eucalyptus* spp. (Myrtaceae), *Lantana camara*, *Vitex negundo* (Verbenaceae), *Cymbopogon* spp. (Gramineae), *Mentha piperita* (Labiatae), *Tagetes minuta* (Compositae) and some other plant products have been studied extensively in recent years [29]. Smoke produced by burning of dried leaves of various plants has been used for protection against mosquitoes since ancient times [29–32]. The major advantages of plant-based traditional repellents are that they are inexpensive, easily available, locally known, and culturally acceptable [31].

Methods Against Aquatic Mosquito Stages (Larval Control)

Mosquitoes go through four stages in their life cycle: egg, larva, pupa, and imago. The first three stages are aquatic. Adult females lay 50–200 eggs per oviposition. The eggs are quite small (*c.* 0.5×0.2 mm^2) and are laid singly and directly on water. Mosquito larvae, commonly called 'wigglers,' live in water for 4–14 days, depending on the water temperature.

The pupa is comma-shaped. The head and thorax are merged into a cephalothorax, with the abdomen curving around underneath. It is a resting, non-feeding stage. The imago (adult, sexually mature insect) is the final stage of development. Most of the malaria vector *Anopheles* species prefer breeding sites that are small, numerous, scattered, and shifting. Each species has its own idiosyncratic preferences, and so detailed knowledge of the specific kinds of water exploited by the local vectors is needed [33]. Larval control (by chemical and non-chemical means) is relevant and a viable method of vector control only if a high proportion of the breeding sites within the mosquito flight range can be located and are accessible, and the breeding sites are of manageable size.

Chemical Larviciding

Paric green (cupric acetoarsenite) was used in the successful eradication of *Anopheles gambiae* in Brazil in the 1930s, but it is an arsenical compound and is too toxic to comply with modern standards. Temephos is much safer, but it also kills insect predators of mosquitoes [34]. Recently, numerous insect growth regulators (IGRs) have been synthesized and used for mosquito control. Typically, these substances are mimics of juvenile hormones, and act by binding to juvenile hormone receptors in the immature form of an insect, preventing its survival to the next stage of development. IGRs are target-specific, and almost all IGRs have a good margin of safety for most non-target organisms, including invertebrates, fish, and birds. They are also relatively safe for humans and domestic animals [35].

Biological Control

Biological control agents have mainly been developed against aquatic mosquito stages, especially the larva and pupa, and not for adults. Biological control refers to the introduction or manipulation of organisms to suppress vector populations. A wide range of organisms help to regulate mosquito populations naturally, through predation, parasitism, and competition [36]. Larval control can be achieved by environmental management and the use of larvicides or larvivorous fish. The aim is generally to kill larvae without polluting the environment.

Larvivorous fish have been used for over 100 years in mosquito control. *Gambusia affinis* has been widely used to control the immature stages of various vector mosquitoes. Other fish species include *Tilapia* spp., *Poecilia reticulata*, and Cyprinidae [37]. The benefits of larvivorous fish are that the mosquito larvae cannot build up physiological resistance, and the fish populations are generally self-sustaining and do not depend on the presence of larvae [38]. Even if some *Anopheles* larvae survive despite the presence of fish, these emerge as smaller adults [39]. The fish are relatively inexpensive, and 6 months after stocking the larger fish can be harvested, providing a sustainable source of income and protein for rural farmers [40].

To minimize the dependency on chemical insecticides, efforts have been made to search for and develop alternative methods for the control of vector mosquitoes. In this respect, various biological control agents have been thoroughly investigated with the support of the United Nations Development Programme/World Health Organization Special Programme for Research and Training in Tropical Diseases. In the last decade, the bacillus-based mosquito larvicides popularly known as biocides or biolarvicides have become popular in vector control. Certain types of bacteria, especially *Bacillus thuringiensis* var. *israelensis* and *Bacillus sphaericus*, have been found to be highly effective for the control of larvae of mosquitoes [41] at very low doses. These bacteria are Gram-positive, soil-dwelling, and commonly used as a biological pesticide; alternatively, the Cry toxin may be extracted and used as a pesticide. They also occur naturally in the guts of caterpillars of various types of moth and butterfly, as well as on the dark surfaces of plants. During sporulation, many strains produce crystal proteins (proteinaceous inclusions), called δ-endotoxins, that have insecticidal action [42]. Upon completion of sporulation, the parent bacterium lyses to release the spore and the inclusions; the toxins exist as inactive protoxins. When the inclusions are ingested by insect larvae, the alkaline pH solubilizes the crystal, and the protoxin is then converted to an active toxin. It has been indicated that the activated toxin binds to insect-specific receptors exposed on the surface of the plasma membrane of midgut epithelial cells, and then inserts into the membrane to create transmembrane pores that cause cell swelling and lysis, and eventually the death of the insect. The major advantages of biolarvicides are reduced application costs, and safety for the environment, humans, and non-target organisms [41].

The application of larvicides may not be an appropriate control strategy in terms of cost-effectiveness, owing to widespread breeding reservoirs; their effectiveness is maintained for only a few days, necessitating frequent and repeated applications at least at the end of every week [43]. Finally, biocides are effective against mosquito larvae but cannot control the pupal stage.

Other than bacteria and fish, many other biological control agents have been evaluated against larval stages of mosquitoes, including mermithid nematodes such as *Romanomermis culicivorax* [44], microsporidia such as *Nosema algerae* [45], and several entomopathogenic fungi [46].

Among these fungi, the oomycete *Lagenidium giganteum* has been proven to be successful for vector control in rice fields [47] and has been commercialized recently.

Source Reduction

'Environmental management' is defined by the report of the Expert Committee as 'The planning, organizing, carrying out and monitoring of activities for the modification and/or manipulation of environmental factors or their interaction with man with a view to prevent or minimize vector propagation and reducing man–vector–pathogen contact.' It includes the building of settlements away from vector sources, mosquito-proofing of houses, personal protection and hygiene measures against vectors, the provision of such installations as mechanical barriers and facilities for water supply, waste water and excreta disposal, laundry, bathing and recreation to prevent or discourage human contact with infested waters, and zooprophylaxis, the strategic placement of cattle as a buffer between mosquito breeding places and areas of human habitation to divert vectors away from the human blood source. The term 'modification' refers to permanent or long-lasting physical transformation of land, water, and vegetation, including drainage, filling, land levelling and transformation, and multipurpose reservoir margins. Although these works are usually of a permanent nature, proper operation and adequate maintenance are essential for their effective functioning. Environmental 'manipulation' is defined as 'any planned recurrent activity aimed at producing temporary conditions unfavourable to the breeding of vectors in their habitats' [48], including water salinity changes, stream flushing, regulation of the water level in reservoirs, dewatering or flooding of swamps or boggy areas, vegetation removal, shading, and exposure to sunlight.

Genetic Control

Genetically modified mosquitoes (GMMs)

In the last decade, molecular biology has been a source of great hope for the creation of GMMs. Genetic control offers a unique opportunity to control vector-borne diseases, particularly malaria [49]. The aim of GMM applications is to suppress or manipulate vector mosquito populations by reducing their ability to transmit diseases [50]. Site-specific gene recombination technologies insert the antipathogen effector genes in the integration sites of the genome, making it more effective [49], and as a result reared sterile mosquitoes can be released into the environment [50].

Sterile insect technique is a species-specific and environmentally non-polluting methodology that relies mainly on the release of large numbers of sterile insects [51,52]. Mating of released sterile males with native females leads to a decrease in the females' reproductive potential, and ultimately leads to local elimination or suppression of the vector population. Field trials in the 1970s and 1980s demonstrated the effect of sterile insect technique against mosquitoes, even with the technology then available [53,54]. For instance, *Anopheles albimanus* was successfully controlled by the use of chemosterilized mosquitoes during a trial in El Salvador [55].

Major Issues and Challenges in Malaria Elimination: the Need for More Commitment

Chemical control remains an important element in the integrated approach to vector control. In this perspective, vector resistance is a major threat to the successful prevention and control of malaria. The number of available and effective insecticides for malaria vector control is decreasing. Currently, only the pyrethroid class of insecticides is appropriate for ITN impregnation and long-lasting insecticide nets [56], but vector mosquitoes have already developed resistance to pyrethroids in some areas of the world [20]. Although 12 insecticides are currently recommended by the WHO for IRS, they belong to only four chemical classes, namely organochlorines, pyrethroids, carbamates, and organophosphates, and cross-resistance among insecticides is frequent [3]. For public health use, it is essential that alternative insecticides belonging to new or different classes be developed if current scaling-up efforts are to be sustained and if local interruption of malaria transmission is to be achieved [3]. Points to be remembered while implementing

TABLE 2. Points to be remembered when implementing effective vector control interventions

Depending on feasibility and availability, indoor residual insecticide spraying, long-lasting insecticidal nets or a combination of both interventions is often the key method to reduce transmission in residual or new active foci
The insecticide and frequency of application of indoor residual spraying are determined by the local epidemiological situation
Up-to-date information is needed on vector resistance to pesticides, especially in conjunction with their continuing extensive use in agriculture. Planning and operations are guided by geographical reconnaissance
Larviciding may play an important supportive or even leading role in some special settings such as arid environments where mosquito breeding sites—often a result of human activity—are few in number and well identified. Larviciding may also be used to reduce receptivity in recent foci

TABLE 3. Technical issues in deploying genetically modified mosquitoes

Funding and regulatory constraints that influence how rapidly new control tools can be developed
Anticipated economic, environmental, health and social trade-offs associated with the use of different control methods
Social and cultural issues expected to influence acceptance of these methods

effective vector control interventions are summarized in Table 2.

GMM research has already yielded the proof-of-principle demonstration that malaria-resistant mosquitoes can be produced, and that induced sterility can be generated. However, deployment of the laboratory-derived genetically engineered mosquito strains effectively in the field remains to be demonstrated, and many challenges remain unmet. These challenges encompass several technical issues, as listed in Table 3. In the case of a new technology such as GMM, careful planning and preparation are also required to address these challenges [50].

No single malaria control measure is sufficient to reduce malaria in any given setting. However, if an entire package of locally appropriate interventions can reach a sufficient level of coverage, then it may be possible to reduce the burden of malaria and achieve the malaria-related Millennium Development Goals [57]. Proper understanding of the local transmission dynamics is the key for the selection of the most appropriate control measure. Good knowledge of the breeding, resting and feeding behaviour of the local vectors must be well documented before an intervention is selected. Baseline information should be collected before initiation of an intervention for proper monitoring and evaluation. To reduce unnecessary costs, countries should first stratify malaria transmission according to the major eco-epidemiological types, before deciding on which intervention measures to be applied and where they are to be applied.

Conclusions

At present, malaria control and elimination is one of the most challenging and serious tasks, owing to the spread of multidrug-resistant strains of *Plasmodium falciparum*, poverty, fragile health infrastructure, insecticide resistance, and ecosystem degradation. However, vector control is one of the most powerful weapons in the process of managing vector populations to reduce/interrupt the transmission of disease. The existing vector control interventions offer highly encouraging results, and have afforded a unique opportunity to eliminate malaria in a few countries. Over the decades, integrated vector management has become vital to antimalarial efforts throughout the world's tropical regions, and is still the most feasible, workable and viable approach.

At present, malaria control relies heavily on a limited arsenal: artemisinin derivatives and pyrethroids. However, these could also become ineffective, owing to the development of resistance. In this perspective, innovative user-friendly and environment-friendly alternatives to conventional vector control are apparently inevitable. The exploration and development of novel and powerful contextual community-based vector control interventions are also warranted. Continuous effort is needed in terms of research and development to improve the existing interventions, such as vector control, diagnosis, treatment, vaccines, biocontrol of vectors, environmental management, and surveillance, for the sustainable elimination of malaria and possible eventual eradication in the near future.

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Transparency Declaration

The author declares that he has no conflict of interest.

References

1. World Health Organization. *World malaria report 2010*. Geneva: WHO, 2010.
2. World Health Organization. *World malaria report 2008*. Geneva: WHO, 2008.
3. World Health Organization. Global malaria control and elimination: report of a technical review. Global Malaria Control and Elimination Meeting (2008). Available at: http://malaria.who.int/docs/elimination/MalariaControl EliminationMeeting.pdf (last accessed 4 March 2010).
4. World Health Organization. Malaria control in countries where time-limited eradication is impracticable at present. Technical Report Series 537. Geneva: WHO, 1974.

5. World Health Organization. *Malaria elimination: a field manual for low and moderate endemic countries*. Geneva: WHO, 2007.
6. Roll Back Malaria. *World malaria day 2010: Africa update*. Progress & Impact Series. World Health Organization, Geneva, 2010.
7. Pluess B, Tanser FC, Lengeler C, Sharp BL. Indoor residual spraying for preventing malaria. *Cochrane Database Syst Rev* 2010; 4: CD006657.
8. World Health Organization. Global Malaria Programme. Indoor residual spraying. Use of indoor residual spraying for scaling up global malaria control and elimination. Geneva: WHO, 2006.
9. Gratz NG. Space sprays for the control of *Aedes aegypti* in South-East Asia and the Western Pacific. *Dengue Bull* 1999; 23. Available at: http://www.searo.who.int/en/Section10/Section332/Section521_2439.htm (last accessed 12 June 2011).
10. World Health Organization. *World malaria report 2005*. Geneva: WHO, 2005. Available at: http://rbm.who.int/wmr.2005 (last accessed 31 December 2010).
11. Hill J, Lines J, Rowland M. Insecticide-treated nets. *Adv Parasitol* 2006; 61: 77–128.
12. Zaim M, Jambulingam P. Global insecticide use for vector-borne disease control. WHO/CDS/NTD/WHOPES/GCDPP/2007.2. 2007.
13. Phillips-Howard PA, Nahlen BL, Wannemuehler KA *et al.* Impact of permethrin-treated bed nets on the incidence of sick child visits to peripheral health facilities. *Am J Trop Med Hyg* 2003; 68 (4 suppl): 38–43.
14. Lengeler C. *Insecticide-treated bednets and curtains for preventing malaria (Cochrane Review)*. Oxford: Update Software, 2002.
15. ter Kuile FO, Terlouw DJ, Kariuki SK *et al.* Impact of permethrin-treated bed nets on malaria, anaemia, and growth in infants in an area of intense perennial malaria transmission in western Kenya. *Am J Trop Med Hyg* 2003; 68 (4 suppl): 68–77.
16. Guyatt HL, Snow RW. The epidemiology and burden of *Plasmodium falciparum*-related anemia among pregnant women in Sub-Saharan Africa. *Am J Trop Med Hyg* 2001; 64: 36–44.
17. Steketee RW, Nahlen BL, Parise ME, Menendez C. The burden of malaria in pregnancy in malaria-endemic areas. *Am J Trop Med Hyg* 2001; 64: 28–35.
18. WHO/AFRO. A policy framework for malaria prevention and control during pregnancy in the African region December 19, 2003. Final Draft, Available from WHO/AFRO. 2004.
19. Hawley WA, Phillips-Howard PA, ter Kuile FO *et al.* Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. *Am J Trop Med Hyg* 2003; 68 (4 suppl): 121–127.
20. Trape JF, Tall A, Diagne N *et al.* Malaria morbidity and pyrethroid resistance after the introduction of insecticide-treated bednets and artemisinin-based combination therapies: a longitudinal study. *Lancet Infect Dis* 2011. DOI:10.1016/S1473-3099(11)70194-3. [Epub ahead of print].
21. World Health Organization. Malaria control today. Current WHO Recommendations. Working document March 2005. Geneva:Roll Back Malaria Department, WHO, 2005.
22. Brown M, Hebert AA. Insect repellents: an overview. *J Am Acad Dermatol* 1997; 36: 243–249.
23. Zadikoff CM. Toxic encephalopathy associated with use of insect repellent. *J Paediatr* 1979; 95: 140–142.
24. Ronald EH, Jan JE, Rigg JM. Toxic encephalopathy in child after brief exposure to insect repellent. *Can Med Assoc J* 1985; 132: 155–156.
25. Karunamoorthi K, Sabesan S. Field trials on the efficacy of DEET impregnated anklets, wristbands, shoulder, and pocket strips against mosquito vectors of disease. *Parasitol Res* 2009; 105: 641–645.
26. Karunamoorthi K, Sabesan S. Laboratory evaluation of dimethyl phthalate treated wristbands against three predominant mosquito (Diptera: Culicidae) vectors of disease. *Eur Rev Med Pharmacol Sci* 2010; 14: 443–448.
27. Karunamoorthi K, Ramanujam S, Rathinasamy R. Evaluation of leaf extracts of *Vitex negundo* L. (Family: Verbenaceae) against larvae of *Culex tritaeniorhynchus* and repellent activity on adult vector mosquitoes. *Parasitol Res* 2008; 103: 545–550.
28. Sukumar K, Perich MJ, Boobar LR. Botanical derivatives in mosquito control: a review. *J Am Mosq Cont Assoc* 1991; 7: 210–237.
29. Karunamoorthi K, Ilango K, Endale A. Ethnobotanical survey of knowledge and usage custom of traditional insect/mosquito repellent plants among the Ethiopian Oromo ethnic group. *J Ethnopharmacol* 2009; 125: 224–229.
30. Mittal PK, Subbarao SK. Prospects of using herabal products in the control of mosquito vectors. *ICMR Bull* 2003; 33: 1–11.
31. Karunamoorthi K, Mulelam A, Wassie F. Laboratory evaluation of traditional insect/mosquito repellent plants against *Anopheles arabiensis*, the predominant malaria vector in Ethiopia. *Parasitol Res* 2008; 103: 529–534.
32. Karunamoorthi K, Mulelam A, Wassie F. Assessment of knowledge and usage custom of traditional insect/mosquito repellent plants in Addis Zemen Town, South Gonder, North Western Ethiopia. *J Ethnopharmacol* 2009; 121: 49–53.
33. Enayati A, Lines J, Maharaj R, Hemingway J. Suppressing the vector. In: Feachem RGA, Phillips AA, Targett GA, eds. *Shrinking the Malaria Map: A Prospectus on Malaria Elimination*. San Francisco: The Global Health Group, 2009; 140–154.
34. World Health Organization. Vector control for malaria and other vector-borne diseases. Report of a WHO Study Group. WHO Technical Report Series 857, World Health Organization, Geneva. 1995.
35. Mulla MS. The future of insect growth regulators in vector control. *J Am Mosq Control Assoc* 1995; 11 (2 Pt 2): 269–273.
36. Chandra G, Bhattacharjee I, Chatterjee SN, Ghosh A. Mosquito control by larvivorous fish. *Indian J Med Res* 2008; 127: 13–27.
37. Lacey LA, Lacey CM. The medical importance of Riceland mosquitoes and their control using alternatives to chemical insecticides. *J Am Mosq Control Assoc* 1990; 2 (suppl): 1–93.
38. Wright JW, Fritz RF, Haworth J. Changing concepts of vector control in malaria eradication. *Annu Rev Entomol* 1972; 17: 75–102.
39. Bond JG, Arredondo-Jimenez JI, Rodriguez MH, Quiroz-Martinez H, Williams T. Oviposition habitat selection for a predator refuge and food source in a mosquito. *Ecol Entomol* 2005; 30: 255–263.
40. Howard AFV, Zhou G, Omlin FX. Malaria mosquito control using edible fish in western Kenya: preliminary findings of a controlled study. *BMC Pub Health* 2007; 7: 199.
41. Mittal PK. Biolarvicides in vector control: challenges and prospects. *J Vector Borne Dis* 2003; 40: 20–32.
42. Roh JY, Choi JY, Li MS, Jin BR, Je YH. *Bacillus thuringiensis* as a specific, safe, and effective tool for insect pest control. *J Microbiol Biotechnol* 2007; 17: 547–559.
43. Karunamoorthi K. Systems thinking: prevention and control of Japanese encephalitis—'the plague of the orient'. In: Ruzek D, ed. *Flavivirus Encephalitis*/Book 1. Intech Open Access Publisher. Croatia. 2011. In press.
44. Zaim M, Ladonni H, Ershadi MRY *et al.* Field application of *Romanomermis culicivorax* (Mermithidae: Nematoda) to control anopheline larvae in southern Iran. *J Am Mosq Control Assoc* 1988; 4: 351–355.
45. Undeen AH, Dame DA. Measurement of the effect of microsporidian pathogens on mosquito larval mortality under artificial field conditions. *J Am Mosq Control Assoc* 1987; 3: 91–93.
46. Federici BA. The future of microbial insecticides as vector control agents. *J Am Mosq Control Assoc* 1995; 11: 260–268.
47. Hallmon CF, Schreiber ET, Vo T, Bloomquist MA. Field trials of three concentrations of Laginex TM as a biological larvicide compared to VectobacTM-12AS as a biocontrol agent for *Culex quinquefasciatus*. *J Am Mosq Control Assoc* 2000; 16: 5–8.

48. Environmental Management for Vector Control. Third Report of the WHO Expert Committee on Vector Biology and Control. Technical Report Series No. 649. World Health Organization, Geneva, 1980.
49. Amenya DA, Bonizzoni M, Isaacs AT *et al.* Comparative fitness assessment of *Anopheles stephensi* transgenic lines receptive to site-specific integration. *Insect Mol Biol* 2010; 19: 263–269.
50. World Health Organization. *Progress and prospects for the use of genetically modified mosquitoes to inhibit disease transmission*. Geneva: WHO, 2009.
51. Dyck V, Hendrichs J, Robinson A (eds). *Sterile insect technique: principles and practice in area-wide integrated pest management*. Dordrecht: Springer, 2005.
52. Knipling E. Possibilities of insect control or eradication through use of sexually sterile males. *J Econ Entomol* 1955; 48: 459–462.
53. Benedict MQ, Robinson AS. The first releases of transgenic mosquitoes: an argument for the sterile insect technique. *Trends Parasitol* 2003; 19: 349–355.
54. Klassen W, Curtis C. History of the sterile insect technique. In: Dyck V, Hendrichs J, Robinson A, eds. *Sterile insect technique: principles and practice in area-wide integrated pest management*. Dordrecht: Springer, 2005; 3–36.
55. Lofgren CS, Dame DA, Breeland SG *et al.* Release of chemosterilized males for the control of *Anopheles albimanus* in El Salvador. III. Field methods and population control. *Am J Trop Med Hyg* 1974; 23: 288–297.
56. USAID. Integrated vector management programs for malaria control. Programmatic environmental assessment. Bureau for Global Health, United States Agency for International Development, RTI International, Durham, NC, USA, 2007.
57. Smith DL, McKenzie FE, Snow RW, Hay SI. Revisiting the basic reproductive number for malaria and its implications for malaria control. *PLoS Biol* 2007; 5: e42.