INTRODUCTION

Despite national and international efforts, malaria remains one of the most serious vector-borne diseases in the world, especially in tropical regions of Africa which accounts for 90% of all malaria-related deaths. After several decades of intensive research on malaria candidate vaccines, only the RTS,S/AS01 vaccine that targets the pre-erythrocytic stages of Plasmodium falciparum has received a positive assessment by the European Medicines Agency. While outcomes of RTS,S/AS01 on infected children aged 6 weeks to 17 months are encouraging, this candidate vaccine should be used as a supplementary tool in immunization programmes to overcome the burden of malaria transmission. Indeed, other vaccines against P. vivax are continually under development. Anopheles funestus are the major malaria vectors in Africa. The first three are members of the An. gambiae complex, which also includes other species such as An. bwambae, An. melew, An. merus, An. quadriannulatus and An. amharicus displaying behavioral, ecological and genetic differences that can influence their vectorial capacity. Anopheles funestus belongs to the Funestus group, which includes 13 African species, viz. An. funestus, An. funestus-like, An. aruni, An. confusus, An. parenisia, An. vaneedeni, An. longipalpis type C, An. leesoni, An. longipalpis type A, An. rivulorum, An. rivulorum-like, An. brucei, and An. fuscivenosus. Apart from An. funestus, the role of other African species of the Funestus group in malaria transmission appears mainly negligible. Historically, control of mosquito populations with insecticides such as dichlorodiphenyltrichloroethane (DDT) has witnessed highest success. However, these efforts have not been sustained due to financial restrictions in programme funding and the emergence of physiological and behavioral resistance in vector populations. It is now widely accepted that thorough knowledge of the transmission cycles and the ecology of vector populations are essential for effective vector control in the long-term, however genetics and population genetics data are also important.

Anopheles gambiae, An. coluzzii, An. arabiensis and Anopheles funestus are the major malaria vectors in Africa. The first three are members of the An. gambiae complex, which also includes other species such as An. bwambae, An. melew, An. merus, An. quadriannulatus and An. amharicus displaying behavioral, ecological and genetic differences that can influence their vectorial capacity. Anopheles funestus belongs to the Funestus group, which includes 13 African species, viz. An. funestus, An. funestus-like, An. aruni, An. confusus, An. parenisia, An. vaneedeni, An. longipalpis type C, An. leesoni, An. longipalpis type A, An. rivulorum, An. rivulorum-like, An. brucei, and An. fuscivenosus. Apart from An. funestus, the role of other African species of the Funestus group in malaria transmission appears mainly negligible. Historically, control of mosquito populations with insecticides such as dichlorodiphenyltrichloroethane (DDT) has witnessed highest success. However, these efforts have not been sustained due to financial restrictions in programme funding and the emergence of physiological and behavioral resistance in vector populations. It is now widely accepted that thorough knowledge of the transmission cycles and the ecology of vector populations are essential for effective vector control in the long-term, however genetics and population genetics data are also important.

ABSTRACT

Over the past decade, global malaria-related mortality has declined dramatically because of combined international actions that have defined and prioritized national and regional efforts to reduce the incidence of malaria, with the ultimate goal of eradication. Vector control strategies using insecticide-treated nets (ITNs) and indoor residual spraying (IRS) in African countries have contributed significantly to the declining incidence of malaria. However, the effectiveness of malaria control is threatened by increasing insecticide resistance and behavioral changes in Anopheles vectors. Thus, there is an urgent need to ensure that future programmes are designed to address these threats and protect the progress made so far in controlling malaria. This review summarizes the current malaria vector control tools and discusses about the critical threats to vector control programme and vector management.

Key words Anopheles; behavioral changes; insecticide resistance; malaria; vector control
to understand the insect adaptive response to insecticides. However, a prerequisite for developing suitable vector control tools is to accurately identify vectors involved in malaria transmission. Since it is feasible, focus is needed on how Anopheles populations respond to vector control measures, so that effective management of malaria vector control can be planned.

Insecticide-treated bednets (ITNs) and indoor residual spraying (IRS) have been widely used as front-line tools against malaria vectors in endemic African regions. These preventive measures are highly effective against malaria vectors, which prefer to bite and rest inside the rooms. Use of ITNs and IRS over the last decade has led to a significant decrease in malaria transmission in many areas of sub-Saharan Africa. Moreover, after the Bill and Melinda Gates Foundation and the Director General of WHO called for malaria eradication as a public health priority, hope of worldwide malaria eradication was renewed and a research agenda to improve malaria research policy and provide substantial recommendations has been proposed. For this purpose, the international community has ambitiously united to control malaria nationally and regionally, with the long-term goal of malaria eradication. While the gains have been massive in many areas of sub-Saharan Africa, they are worryingly fragile and signs of malaria resurgence have emerged in some areas. Nevertheless the World Health Assembly has adopted the Global Technical Strategy for Malaria 2016–30 with the goal of decreasing malaria burden by 90% over the next 15 yr based on several schemes, including surveillance, monitoring and evaluating malaria systems control.

This review was focused on current vector control strategies and the adaptive responses of Anopheles vectors in African countries that challenge the ability to sustain and consolidate the substantial gains made so far.

Data source

The search terms “malaria”, “Africa”, “insecticide resistance”, “behavior changes”, and “Anopheles” were used in the online databases like PubMed, Web of Science, and Google Scholar to conduct a literature search and to screen published research articles. To identify global research on the historical aspects of malaria control strategies, the articles and review published on any date in English and French were read and scanned. The full articles that described the primary vector control tools and their impact on insecticide resistance status and behavioral changes in malaria vectors were screened.

An online mapping tool, IR mapper was used to reproduce a map on the repartition of the insecticide resistance in the main malaria vectors in sub-Saharan Africa according to the World Health Organization (WHO) susceptibility test and the Centers for Disease Control and Prevention (CDC) bottle assay. Map was created from data collected from 2000 to 2015.

The online database, PubMed was also used to index articles published in the last 16 years (2000 to 2015) to assess the trend on the number of papers on the insecticide resistance of Anopheles vector in Africa published per year.

Control strategies against malaria vectors

Malaria vector control strategies target both the immature and adult stages of Anopheles populations. Before World War II, antilarval malaria control was the preferred strategy to control malaria. The intervention strategies predominantly included physical elimination of mosquito breeding sites, biological control using larvivorous fish and chemical larviciding with Paris green. Today, larval control is used and promoted to limit the development of Anopheles larvae in breeding sites using biological larvicides such as Bacillus thuringiensis israelensis (Bti) that were first developed 30 yr ago. However, larval control is not particularly effective, especially in case of some Anopheles species for which breeding sites are extremely numerous and inaccessible.

Vector control strategies have evolved considerably since Müller’s discovery of the insecticidal properties of DDT in the 1939 (Fig. 1). The most advanced and efficient techniques targeted adult female mosquitoes. IRS had been identified as a suitable approach for malaria eradication programmes between 1955 and 1969. During this period, the large-scale use of DDT in many countries across the world led to a dramatic reduction in malaria transmission in the United States, European countries, South East Asia, India and South America. As a result, many malaria experts believed that it was not necessary to continue IRS programmes with DDT. Nonetheless, in areas that were not routinely monitored, these successes have not been maintained due to operational problems, financial restrictions, the exophilic behavior of vectors and, mainly, insecticide resistance. These phenomena have contributed to a resurgence of the disease in many places in South America, South East Asia and Eastern Europe where it had previously declined.

Eradication programmes had not been planned for sub-Saharan Africa due to the long transmission season and the extremely high degree of malaria endemicity. However, a number of malaria pilot projects were established in some areas between the 1940s and the 1960s to interrupt malaria transmission. A significant reduction in malaria transmission and vector populations were re-
corded in South African countries immediately after the introduction of malaria control measures. However, during the mid-1980s, malaria transmission rose again and severe outbreaks were recorded. In West and East African regions, the control methods were not sufficient to interrupt malaria transmission. Thus, the attempt to eliminate malaria in Africa was globally considered as failure.

In the 1980s, pyrethroids, a new family of chemical compounds, were added to the arsenal of public health insecticides to treat houses and especially to impregnate mosquito nets. From 2000–15, malaria vector control programmes have shifted towards the use of pyrethroid-treated bednets. The main aim of ITNs is to decrease the level of contact between human populations and the *Anopheles* vector, thus reducing the vector’s feeding frequency and daily survival rates. In sub-Saharan Africa, the estimated proportion of the population who has access to an ITN has increased substantially from <2% in 2000 to 67% in 2015 (Fig. 2). The introduction of pyrethroid-treated bednets has also impacted entomological parameters, such as decrease in vector abundance, parity and infection rates in *Anopheles* populations causing a decline in the vectorial capacity of *Anopheles* populations, and consequently reduction in the malaria-associated morbidity and mortality in African countries. Despite these gains, malaria resurgence has been noted in some areas in Senegal, Western Kenya, and Gambia where ITNs have been used, and in some parts of Benin, Tanzania and Uganda following IRS coverage. This situation sheds doubt on the effectiveness of current vector control tools and highlights the need to better understand the main threats, such as...
resistance to insecticides and the behavioral changes of these vectors.

Insecticide resistance mechanisms in *Anopheles* vectors

Malaria vector control strategies such as IRS and ITNs reduce the vectorial capacity of *Anopheles* vectors and thus malaria transmission; these two strategies were the central pillars of malaria control from 2000–15. During this period, *Anopheles* vector resistance has spread in major insecticide classes used for malaria vector control in African countries (Fig. 3) according to data extracted from the online mapping tool IR mapper. At the same time, published papers on the insecticide resistance of *Anopheles* vectors in Africa have gradually increased (Fig. 4), suggesting that insecticide resistance is an evolving phenomenon that attracts more and more attention. Resistance can arise from any change that blocks or interferes with the insecticide’s mechanism of action, including changes to how the mosquito absorbs or degrades insecticide molecules and modifications to the insecticide target site.

The mechanisms of resistance vary widely, as target sites and mechanisms of degradation can differ among insecticides. Most of the synthetic insecticides used for vector control intended to protect public health are organophosphates, organochlorines, carbamates and pyrethroids. These classes of insecticides mainly target receptors in the mosquito’s nervous system or inhibit enzymes involved in transmitting nerve impulses, causing paralysis and insect death. Some target sites are shared by different classes of insecticides. DDT and pyrethroid insecticides act through the receptor for the voltage-dependent sodium channel (CNaVdp), organophosphates and carbamates target acetylcholinesterase (AChE), and cyclodiene insecticides target the gene coding for the gamma-aminobutyric acid (GABA) receptor. Resistant strains have mutations in target sites or genes that code for enzymes that impact the effectiveness of a specific insecticide. Thus, cross-resistance is a great concern given that there is a limited choice of alternative insecticide appropriate for routine use in managing malaria resistance. This is of particular concern for pyrethroids and DDT—Pyrethroids are the only approved option for bednet treatment, and DDT provided it is safely applied using
the recommendations of WHO, is the preferred molecule for indoor residual spraying due to its longer residual efficacy, irritant effect on vectors and low cost. However, predominantly pyrethroid insecticides were used in IRS programmes funded by the U.S. President’s Malaria Initiative in Africa between 2006 and 2010. The programme then switched in recent years to other insecticides due to increasing pyrethroid resistance. Resistant *Anopheles* populations are cross-resistant to both pyrethroids and DDT. Resistance to pyrethroids and DDT seems to be widespread in *Anopheles* malaria vectors, mostly due to two alternative point of mutation at the position 1014 on the voltage-gated sodium channel gene, causing a phenomenon known as knockdown resistance (kdr). In West Africa, kdr resistance results from a phenylalanine substituting for leucine (L1014F); in East Africa it results from a serine substituting for leucine (L1014S). Therefore, the two types of kdr mutations have been named for their geographic locations: L1014F is referred to as kdr-west and L1014S as kdr-east.

In the *An. gambiae* complex, the kdr-west mutation was initially described in *An. gambiae*. It was formerly known as molecular form S, and occurs at a high frequency in Ivory Coast and Burkina Faso. Kdr-west is now widespread in *An. coluzzii* (previously identified as molecular form M) and in its sibling species *An. arabiensis* in West Africa. It also occurs in Tanzania (East Africa) in *An. gambiae*, and *An. arabiensis*. The kdr-east mutation now occurs in the three sibling species throughout West and Central Africa. Based on these observations, the originally described geographic separation between these two alleles no longer holds. Both alleles spread in the vectors of the *An. gambiae* complex across Africa. In addition, an asparagine-to-tyrosine substitution mutation at position 1575 (*N1575Y*) on the voltage-gated sodium channel is responsible for pyrethroid and DDT resistance. It was originally identified in *An. gambiae* (S form) in Burkina Faso. This newly emerged resistance allele has been found at high frequencies in both *An. coluzzii* and *An. gambiae* collected throughout West and Central Africa. Thus, there is an urgent need to look for other substitutions in the sodium channel that could yield insecticide resistance in malaria vectors.

Even more disturbing is evidence from Burkina Faso in 2013, that *An. gambiae* strains that are resistant to DDT and pyrethroids are more susceptible to *P. falciparum* infection at both the oocyst and sporozoite stages than insecticide-susceptible strains. Another study conducted in 2016 in Tanzania has reported a rate of infection with *P. falciparum* three times higher in resistant *An. gambiae* s.s. populations than in populations susceptible to deltamethrin. This remains a great concern for the epidemiology of malaria, as malaria transmission could be exacerbated by the increasing proportion of infected mosquitoes that come in contact with humans. However, Kristan et al. showed that exposure of a resistant Ugandan population of *An. gambiae* to sub-lethal dose of deltamethrin inhibited the growth of *P. falciparum* compared to populations exposed to untreated nets. To understand these conflicting findings on the vectorial competence of resistant *Anopheles* populations, future research needs to focus on the interaction between vector and parasite in the context of the spread of insecticide resistance via different mechanisms.

*Anopheles* populations are also developing resistance to carbamate and organophosphate insecticides that are established alternative molecules to pyrethroids for adult vector control. Resistance to organophosphates and carbamates due to insensitive AChE in malaria vectors results to a glycine-to-serine substitution at the amino acid position 119 (mutation G119S). Since, the first report in 1994 of decreased sensitivity to carbamates in *An. gambiae* populations from Ivory Coast, a molecular test has been developed to identify the G119S mutation. This mutation, also named *Ace.1 G119S* or *ace-1* mutation, has been detected in sympatric *An. gambiae* and *An. coluzzii* populations in different parts of Burkina Faso and Southern Ghana, with higher frequencies in *An. gambiae*. In Ivory Coast, the *Ace.1 G119S* mutation is found at high frequencies in both *An. gambiae* and *An. coluzzii*. Subsequent studies performed in 2014 have also reported it in *An. arabiensis* populations in Burkina Faso. Another mechanism conferring resistance to organophosphate and carbamate compounds is an *ace-1* gene duplication that arose from susceptible and resistant alleles located on the same chromosome. The *ace-1* gene has been observed in *An. coluzzii* and *An. gambiae* populations in Ivory Coast and Burkina Faso. Previous studies have reported a fitness cost that reduces some biological traits such as fecundity, longevity, mating rate, development time and survival of mosquitoes that carry the resistant allele. However Assogba et al. showed that the presence of *ace-1* gene duplication in *Anopheles* populations has allowed a fitness advantage and consequently it has spread in natural populations. This situation complicates the insecticide resistance management strategies given that it will be challenging to revert toward susceptibility when switching to carbamates and organophosphates. Therefore, for vector resistance management strategies to be effective, we need to better understand the fitness costs associated with resistant strains before replacing the insecticides used.

Target site insensitivity, however, is not the only
mechanism of insecticide resistance. Anopheles populations could develop metabolic mechanisms of resistance arising from over-expression or amplification of genes coding for enzymes involved in detoxifying insecticidal compounds. The main enzymes involved in metabolic insecticide resistance belong to the super families of cytochrome P450 monooxygenases (P450s), glutathione S-transferases (GST) and esterases. The P450s are involved in the metabolism of pyrethroid organophosphate and carbamates insecticides, and GSTs in DDT metabolism. Over-expression of esterases increases organophosphate, carbamate and, to a lesser extent, pyrethroid resistance. Metabolic resistance is the most common resistance mechanism in insects, and it has now expanded to Anopheles vectors. Furthermore, multiple enzymes have been described in each super family that display broad substrate specificities indicating that each member of the super family could be involved in the metabolism of one or several insecticides. Indeed, Mitchell et al showed that expression of the gene that codes for CYP6M2, an enzyme previously implicated in pyrethroid resistance in wild-type An. gambiae s.s. populations, is also capable of metabolizing the organochlorine DDT. Thus, it may not be feasible to rely on switching insecticides to manage resistance. Metabolic mechanisms of carbamate resistance have been implicated in populations of An. gambiae that are resistant to DDT and permethrin, thus co-implication of both resistance mechanisms in Anopheles populations at the same geographic location further complicates malaria control efforts. In Benin, Aïkpon et al recently reported carbamate and organophosphate resistance in An. gambiae populations from Atakora that had both the ace-1G119S mutation and high levels of activity of mixed function oxidases.

Unlike the major vectors within the An. gambiae complex, metabolic mechanisms of resistance are primarily implicated for resistance in An. funestus species. Anopheles funestus receives much less attention than An. gambiae, but reports of An. funestus resistance to pyrethroids, DDT and carbamates are increasing in many parts in Africa, including South Africa, in other Southern African countries such as Mozambique, Zambia and in Benin and Senegal in West Africa. Beyond the expression of detoxification enzymes, Riveron et al reported metabolic resistance to DDT in An. funestus populations associated with a point of mutation from leucine to phenylalanine (L119F) in a Glutathione S-Transferase epsilon 2 (GSTe2) gene. Formerly, another An. funestus mutation from alanine residue 302 to a serine (A302S) in the gene coding for the GABA receptor has been associated with dieldrin resistance. However, this resistance results from target site insensitivity, showing that insecticide resistance in An. funestus can not be solely attributed to metabolic mechanisms. This is confirmed by a recent study (2016) conducted by Ibrahim et al that reported a new N458L mutation (N458L) on the exon 4 of the ace-1 gene in An. funestus populations conferring carbamate resistance. Thus, the management of resistance in An. funestus will need to investigate the potential for other mutations that confer both target site insensitivity and detoxification.

Widespread insecticide resistance in Anopheles vectors has arisen in parallel to tremendous expansion in funding and effort of vector control measures in sub-Saharan Africa. The global malaria-control community takes this threat seriously. The Global Plan for Insecticide Resistance Management in malaria vectors (GPIRM) includes operational management strategies based mainly on the rotation, mosaic spraying or mixture of insecticides with different modes of action. Selective pressure is such that cross-resistance between insecticides with the same mode of action and co-involvement of mechanisms such as target site insensitivity and metabolic mechanisms of resistance pose serious operational obstacles to the long-term use of these classes of insecticides. Furthermore, few new insecticides appropriate for public use have been developed, since pyrethroids appeared on the market nearly 40 yr ago. However, none of the recently developed insecticides have been approved to impregnate bed nets or to use for indoor residual spraying. Additionally, the effectiveness of new compounds needs to be evaluated in the field against resistant Anopheles phenotypes. For now, malaria vector control remains complicated, and there is great concern about the risk of reemergence of malaria in certain areas in sub-Saharan Africa.

Changes in behavior and Anopheles population composition

The implementation of insecticide-treated nets and indoor residual insecticide spraying over the past decade has had a real impact on the incidence of malaria infection. Both are primary malaria vector control strategies, because target vector populations bite indoors and rest on walls until eggs are fully developed. Nevertheless, to be successful, the vector-control tools need to be adapted to the local epidemiological context, taking into account vector biology, ecology and behavior. Several studies have demonstrated that Anopheles vectors in African countries are active at night before introduction of intervention measures. Indeed, Dossou-Yovo et al showed that the vast majority of An. gambiae sensu stricto, the species which has recently been split into An. gambiae and
*An. coluzzii*\textsuperscript{13} infected with *P. falciparum* was recorded between 2300 and 0400 hrs in Ivory Coast. Similarly, in Madagascar the bite peaks of *An. gambiae sensu lato* are between 2200 and 0200 (indoors) and 0100 and 0400 hrs (outdoors)\textsuperscript{14}. These authors also demonstrated that most *An. funestus* bites occurred from 0100 to 0300, indoor-sand from 0200 to 0500 hrs, outdoors. Vectors were therefore most aggressive at the same time when humans were immobile (sleeping time). This is why indoor interventions are effective and appropriate tools to protect people against the highly endophagic and endophilic African malaria vectors\textsuperscript{20}.

However, socio-environmental changes like the introduction of effective vector control tools could, in turn, induce a behavioral change in *Anopheles* vectors. Indeed, Badyaev\textsuperscript{115} reported in 2005 that extreme environments can disrupt normal development and exert strong phenotypic selection. In the context of malaria control, both the physical net barrier and insecticidal action induce stress in *Anopheles* mosquitoes by preventing them from taking their blood meal or from resting on walls until their eggs mature\textsuperscript{116-117}. Behavioral modifications could include a change in feeding time, a shift from human to animal feeding, or an increase in exophilic behavior. These behavioral changes could arise because of the selection pressure induced by impregnated mosquito nets, giving vectors that bite early and/or feed outdoors a selective advantage, leading to a phenotypic shift in the population.

A study conducted in 2012 in Ethiopia reported a shift to earlier biting in *An. arabiensis* after the use of permethrin-treated bednets, with 80% of individuals collected before 2200 hrs and with a peak of activity between 1900 and 2000 hrs, when most people are not yet under their bednets\textsuperscript{18}. An early peak in biting behavior has also been described in *An. funestus* in Tanzania after widespread use of ITNs\textsuperscript{119}. In addition, *An. funestus* began to bite more outdoors, and could be responsible for the residual malaria transmission in this area. Residual transmission is defined as all forms of transmission occurring after universal coverage of ITNs or IRS\textsuperscript{20}.

Early evening biting activity has been attributed to the fact that insecticides have an exito-repellent effect, they deter mosquitoes from entering rooms diverting them outside. Females diverted outside display disrupted feeding behavior because they cannot access to host blood, leading to a longer oviposition cycle. These females would be inclined to bite early the following night\textsuperscript{121}. Similar outdoor behavior in *An. funestus* has also been observed in Benin, West Africa, where a great proportion of mosquito populations are active after dawn\textsuperscript{122}. This change in biting behavior was more pronounced in Dielmo, a Senegalese village where *An. funestus* developed diurnal activity with peak aggressiveness between 0700 and 1100 hrs, when people are also active and away from their ITNs\textsuperscript{123}. The *An. funestus* mosquitoes in this study that were active at the new time retained their anthropophagic and endophilic characteristics, preserving a close relationship with the human population and maintaining a malaria transmission risk in this area.

Behavioral change after implementation of vector control strategies is not a new phenomenon but focus is more often on insecticide resistance, even though a slight shift in *Anopheles* behavior can increase the risk of malaria transmission. Githiko *et al*\textsuperscript{124} showed early exophilic behavior of *An. gambiae s.s.* in Kenya after introduction of ITNs, even though this species is known to be primarily endophilic. Moreover, this new phenotype exhibited extreme anthropophagic behavior that raises a major concern in malaria transmission. These findings are consistent with a study in Kenyan coastal areas, where significant proportions of *An. gambiae s.l.* populations developed outdoor biting pattern at earlier evening, in villages when ITNs were used compared to control zones where no nets were used\textsuperscript{111}. However, such observations could result from a change in behavioral patterns or in vector composition following the introduction of ITNs. Indeed, as already mentioned above, *Anopheles* vectors in Africa belong to complexes, or groups of species. Different forms, populations or species may have behavioral differences, thus contributing to malaria transmission at different places, different times or seasons. After vector control interventions, *Anopheles* populations can respond differently to selective pressure, and shifts in species composition including sibling species can be observed. This is a great concern with the efficient malaria vectors *An. gambiae, An. coluzzii and An. arabiensis*, the sibling species of the *An. gambiae* complex that also share a broad sympatric range. *Anopheles gambiae* and *An. coluzzii* are highly anthropophagic vectors\textsuperscript{126} compared to *An. arabiensis*, which also feeds on cattle\textsuperscript{127}. Thus, the introduction of ITNs reduced contact between humans and the vector, eliminating *An. gambiae and An. coluzzii* that are more restricted in their host feeding preferences, leaving *An. arabiensis* at very high densities. This phenomenon was recorded in 2010 in Tanzania in two hyper-endemic malaria transmission areas where coverage of untreated bed nets was already high. The addition of ITNs had a stronger impact on the density and survival of *An. gambiae s.s.* than on *An. arabiensis*\textsuperscript{128}. This observation was not associated with competitive displacing of the anthropophilic species by *An. arabiensis*, but rather with preferential feeding of *An. arabiensis* on animals and shifting to an earlier bit-
ing time, when humans are outdoors and unprotected. However, a shift in species composition was reported in a Kenyan study, where *An. arabiensis* was collected in the greatest proportion (99%) after scale-up of the national ITN programme compared to *An. gambiae* s.s (1%), which had previously been the dominant vector. Similar observation has been observed in a Senegalese village where *An. arabiensis* became the most prevalent species after the implementation of mosquito nets. These phenotypes that exhibit more behavioral plasticity in feeding behavior are not currently a target of control tools, hampering the effectiveness of control strategies. However, mass killing of susceptible mosquitoes provides a selective advantage to non-target species, as they take over the ecological niches and increase in density.

Changes in *Anopheles* vector behavior and species composition can also be responsible for residual malaria transmission, compromising the effectiveness of the major vector control tools that are currently available and threatening the goal of eliminating malaria transmission in endemic African countries.

**CONCLUSION**

Ongoing efforts to control malaria transmission focus largely on indoor interventions such as ITNs and IRS, as both tools reduce human-vector contact and lead to a significant reduction in the feeding frequency and lifespan of vectors. However, the emergence of insecticide-resistant anophelines and their ability to develop diverse resistance mechanisms require better resistance surveillance. Tools to improve surveillance include the development of DNA markers associated with target site mutations and an in-depth understanding of the evolution of gene expression involved in insecticide resistance. Simultaneously, the development of new classes of insecticides is urgently needed to improve the management of insecticide resistance in malaria vectors. Moreover, behavioral shifts to the early and outdoor feeding in the dominant *Anopheles* vectors could jeopardize the success of control operations.

To develop suitable strategies in response to these specific behavioral changes, more genomic studies are needed to understand the mechanisms related to adaptation of *Anopheles* vectors to their changing environment. Although global funding agencies and the governments of endemic countries have recently committed to significantly reduce malaria burden, further research and strategic investment are crucial to understand the evolution of mosquito vectors and to avoid resurgence of malaria transmission in sub-Saharan African countries, where the climate favours *Anopheles* proliferation especially in the areas with precarious healthcare systems.

**Conflict of interest**

The authors declare no conflicts of interest.

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