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Malaria Vector Control Commodities Landscape

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Abbreviations

AIDS	acquired immunodeficiency syndrome
DFID	Department for International Development
EC	emulsifiable concentrate
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMAP	Global Malaria Action Plan
GPIRM	Global Plan for Insecticide Resistance Management
IQK	Insecticide Quantification Kit
IRM	insecticide resistance management
IRS	indoor residual spray (or spraying)
ITN	insecticide-treated net
IVCC	Innovative Vector Control Consortium
LLIN (LN)	long-lasting insecticidal net
LLIRS	long-lasting IRS
NGO	nongovernmental organization
NIH	National Institutes of Health
NMCP	national malaria control programme
OC	organochlorine
OP	organophospate
PMI	President's Malaria Initiative
PQR	Price and Quality Reporting
PY	pyrethroid
RBM	Roll Back Malaria Partnership
R&D	research and development
SC	suspension concentrate
UN	United Nations
UNICEF	United Nations Children's Fund
US	United States
USAID	United States Agency for International Development
US$	United States dollar
UTN	untreated nets
VCAG	Vector Control Advisory Group
WHO	World Health Organization
WHOPES	WHO Pesticide Evaluation Scheme
WP	wettable powder

1 Executive summary

Introduction

This report is part of an ongoing initiative within UNITAID to describe and monitor the landscape for malaria commodities. It focuses on product, technology and market dynamics around malaria vector control products that impact at-risk populations in endemic countries, particularly focusing on insecticide-treated nets (ITNs) and indoor residual spraying (IRS) that are the main interventions currently used for malaria vector control. The report provides an overview of the current ITN and IRS technologies and market landscape as well as a high-level perspective on barriers to delivery and access. Information in this report was collected through a variety of methods, including desk research, literature reviews and expert interviews.

Public health problem

The World Malaria Report 2013 estimated that there were 207 million cases of malaria in 2012 and 627 000 deaths, with over 75% of the deaths occurring in children under 5 years old. The World Health Organization (WHO) estimates that there are approximately 3.2 billion people at risk of contracting malaria. Although the greatest proportion of the total at-risk population lives in Asia, malaria has the greatest health impact in Africa, which accounts for 80% of worldwide cases and 89% of deaths. While there has been progress in recent years with a 25% reduction in cases and a 42% reduction in deaths between 2000 and 2012, the progress falls short of goals to reduce malaria cases by 75% (~56 million cases) by 2015.

Technology landscape

Vector control is one of the primary tools in the prevention and eradication of malaria. Vector control is also used to control other vector-borne neglected tropical diseases such as dengue and leishmaniasis. Vector control can decrease malaria transmission by reducing the overall vector population, shortening its lifespan or by preventing them from biting and feeding.

A range of interventions for vector control is available. WHO provides guidance on the intervention tools that are effective, recommending ITNs, particularly long-lasting insecticidal nets (LLINs), and IRS as the primary tools for control of malaria vectors:

- Bednets:
  - Untreated net (UTN): a net material that acts as a physical barrier between a person and mosquitoes, inhibiting blood feeding and, therefore, transmission.
  - ITN: a mosquito net coated with insecticide by dipping the net in a solution of insecticide and water; the net acts as a physical barrier but also provides additional protection by repelling insects away from the net area and/or by killing insects that come into contact with the net. The insecticide treatment can provide from 6 to 12 months of protective effect, depending on washing and handling, and requires periodic re-treatment.

- LLIN (or LN): a mosquito net with insecticide incorporated within or bound around the net fibre during manufacture. The net provides protection in the same way as an ITN, but retains its biological activity for at least 20 standard washes under laboratory conditions and three years of recommended use under field conditions.
- It is estimated that a UTN has about 50% of the effectiveness in control of malaria transmission compared to an ITN or LLIN.

- IRS: application of chemical insecticides on interior walls and roofs of all houses in a designated area. The primary control effect is by death of vectors that rest on treated surfaces. Some insecticides (e.g. pyrethroids) also act as repellents and deter insects from entering houses, although this effect is considered to be limited in impact.

WHO also recommends the use of other intervention tools, but only in certain situations:

- Larval source management: this includes manipulation of environmental factors to reduce vector breeding sites or use of chemical or biological-based larvicides to kill the larval stage of the mosquito and thus reduce the adult population. WHO only recommends use of larvicides where breeding sites are "few, fixed and findable" and as an addition to either an LLIN or IRS programme.
- Space spraying: spraying an aerosolized insecticide into the air. The treatment kills insects flying in the air at the time of spraying but has no residual effect. Space spraying is recommended by WHO only for use in extreme circumstances for malaria control such as epidemics in urban areas or refugee camps.

A range of consumer products, such as coils, vaporizing mats, aerosol cans, topically applied repellents, etc., is also used to provide protection against mosquito biting. Currently, there are insufficient data to show that these products are able to control malaria transmission. These product forms, therefore, do not carry a WHO recommendation.

Many of the intervention tools rely on insecticides to provide the primary control effect. The most widely used intervention, LLINs, is currently reliant on just one class of insecticide—pyrethroids. The other primary tool, IRS, at present uses four classes of WHO recommended-chemistry—pyrethroids, organophosphates, carbamates and an organochlorine.

Insecticide resistance is a major threat to the effectiveness of these primary vector control tools. Resistance has already developed and is present in varying intensities in all four classes of insecticide. Resistance to pyrethroids is a particular risk, due to the widespread reliance on LLINs to provide vector control, cross-resistance to different insecticides and the multiple mechanisms of resistance that have developed. Currently, the use of an IRS is the only way to apply an alternate class of insecticide to a pyrethroid for adult vector control. Progress on implementing resistance management strategies has been very limited.

The vector control research and development (R&D) pipeline is primarily focused on developing new insecticides to overcome insecticide resistance. The first product from a class with no known resistance to date, an IRS based on a class of insecticide already used in agriculture but not previously used for malaria vector control, is in the final stages of development and evaluation and could be available in the vector control market in 2015. Other resistance-breaking products at earlier stages are in development and could be available in the market from 2017 onwards. R&D projects are also looking for tools to control transmission of malaria caused by residual transmission (such as that caused by outdoor biting). The current status of the R&D pipeline is encouraging but fragile. Vector control is not seen as an attractive target for investment in R&D by private industry—the sector is regarded as relatively small, high risk and price driven with low barriers to entry leading to returns on investment that are insignificant or non-existent.

WHO provides recommendations and specifications on products through the WHO Pesticide Evaluation Scheme (WHOPES). Many countries and donor organizations only purchase products that have been recommended by WHOPES. In addition, early stage new paradigms are evaluated by the Vector Control Advisory Group (VCAG).

Market landscape: ITNs and LLINs

There are approximately 800 million people at risk of malaria in sub-Saharan Africa. Universal coverage, defined as universal access to and use of LLINs, would require approximately 450 million treated nets to be in use each year. Latest estimates suggest there will be between 300 and 400 million nets in use by the end of 2014 depending on the assumptions on net life and distribution that are used. Based on an average net life of three years, approximately 150 million nets need to be delivered every year to Africa to maintain coverage. Based on the rate of LLIN delivery in the first three quarters of 2014, approximately 215 million nets will be delivered to sub-Saharan Africa over the whole year. Since the majority of the at-risk population are underprivileged and poor, virtually all nets in Africa are supplied by donors, either free of charge or at a highly subsidized price in order to guarantee access.

The requirement for and coverage of treated nets in the rest of the world is less clear. Outside of sub-Saharan Africa there are approximately 2.4 billion people at risk of malaria. Around 45% of this population lives in South-East Asia in low transmission areas. At the end of 2013, there were around 80 million donor or publicly provided nets in use outside of Africa. It is believed that some markets outside of Africa have high levels of nets (a combination of UTNs, ITNs and LLINs) purchased directly by users from the private market.

The funding of nets is very concentrated. The Global Fund to Fight Aids, Tuberculosis and Malaria (Global Fund) and the United States President's Malaria Initiative (PMI) account for more than 75% of purchases, with the United Nations Children's Fund (UNICEF), the World Bank and the United Kingdom Department for International Development (DFID) the main purchasers of the remainder in recent years. Based on total deliveries in 2013 of approximately 143 million nets at an approximate price per net of US$ 3.00, the total value of LLINs purchased by donors would be around US$ 430 million. The Global Fund has made some important changes to its strategy and approach on funding and purchase processes for vector control commodities. The New Funding Model allocates funds over a three-year period and gives countries more flexibility on how funds are spent. It is not yet clear what impact there will be, if any, on the level of funds allocated to vector control. The new purchasing processes are designed to drive better value for money and to give suppliers greater visibility of forward demand.

Many suppliers of LLINs have a negative attitude of the market operation. They are frustrated that recent innovative products that have been evaluated and recommended for malaria control have achieved very poor market penetration due to the reluctance of major donors to pay higher prices and, in some cases, a lack of information on where products can be best deployed. According to several manufacturers, LLIN prices have also been driven down to marginal levels of profitability. There is a risk that some suppliers will withdraw from investment in innovation or the market entirely.

Between 2009 and 2013, two companies accounted for approximately 65% of total nets supplied. There are now 10 companies with WHOPES-recommended nets, and a further five suppliers in the evaluation process. Data on the split of supply between manufacturers in the 2013/2014 season are not yet publicly available, but it is believed purchases are more evenly spread across the supplier base. It is estimated the supply capacity for LLINs ranges between 240 and 300 million nets per year.

LLIN prices have fallen by more than 40–45% since 2009, and the purchase price of a standard net is currently around US$ 2.95. Several suppliers claim that returns at this price level are marginal. Taking into account distribution costs, the final cost of a delivered net to a user is estimated at around US$ 5.80 per person. Assuming net life of around three years, the cost of protecting a person with an LLIN is around US$ 1.00 per year.

Distribution of donor-supplied nets is mainly carried out by mass campaigns (87–90%), with the remainder split between routine distribution systems such as antenatal care clinics, immunization clinics and other channels. Mass campaigns have been highly effective in gaining initial coverage levels but may not be the most effective and efficient means of maintaining coverage. To maintain universal coverage with nets, WHO recommends a combination of mass free distribution and continuous distribution through multiple channels.

Market landscape: IRS

Approximately 136 million people were protected by IRS in 2012. Since 2010, there has been a 30% reduction in the number of people protected by IRS. Detailed data on IRS insecticide use in all countries are not available to enable a definitive analysis of the cause of the reduction in use. The increasing problem of resistance to pyrethroids necessitates a rotation of insecticide classes with different modes of action, including more expensive non-pyrethroid alternatives (organophosphate and carbamate). Given relatively fixed budget levels allocated to IRS, this appears to be resulting in a reduction in the number of structures sprayed and people protected.

The largest overall providers of funds for IRS are country governments. Two donor organizations, PMI and the Global Fund, also fund IRS commodities and operations, spending approximately US$ 90 million and US$ 7.5 million, respectively in 2013.

Information on suppliers of IRS insecticides is limited and not well documented. Most of the important active ingredients recommended for use in IRS by WHOPES are produced by several manufacturers. A key issue is whether all manufacturers consistently make products that conform to the WHO specifications for each recommended formulation. Two new IRS products are based on novel slow-release formulations that require specific production equipment and know-how and could limit the number of suppliers able to produce the new products, thereby limiting the potential for a competitive market.

Application of IRS requires major planning, training and operations. Based on a study by PMI, assuming one application is sufficient to provide protection during the whole of the peak transmission season, the cost range to protect one person per year is US$ 2.00–11.00, with an average of US$ 5.00.

Market shortcomings

The main market shortcomings that have been identified are summarized in Table 1.

Table 1: Summary of vector control shortcomings

Category	Shortcoming	Reason
Availability	Lack of new products and paradigms, particularly to address resistance and durability concerns.	■ Manufacturers reluctant to invest in R&D due to: ◆ uncertainty around whether or not there will be a willingness to pay for the innovations, as the market is very price sensitive; ◆ metrics to differentiate innovation in net-based products (e.g. longer efficacy; increased durability; insecticide resistance mitigation) not in place beyond the WHOPES minimum quality standards; ◆ their perception that R&D costs will be difficult to recoup because "me too" equivalent products will undercut reference product prices before R&D investment is paid back and rewarded; ◆ evidence of the health impact and effectiveness of new paradigms will be difficult, expensive and time consuming to generate.
	Innovative products face difficulties reaching the market in a timely fashion.	■ Improved tools to address resistance, durability and outdoor transmission challenges will require at least two to three years in the WHOPES process to reach the market. ■ WHOPES may not have sufficient capacity to operate to a faster timescale while maintaining quality. ■ Interface between VCAG and WHOPES not yet tested. ■ Some delays are caused by manufacturers providing products that are of unsuitable quality for testing. ■ Unclear metrics to differentiate products and measure innovations.
	No products with proven ability to control disease transmission from outdoor biting.	■ Not viewed as priority to date. ■ Work now being funded by the Bill & Melinda Gates Foundation.
Affordability	Higher cost of products for resistance limits uptake.	■ Resistance-breaking tools are more expensive than base pyrethroid treatments. Budgets are limited, resulting in reduced coverage or continued use of pyrethroids. ■ Insufficient large-scale use data to demonstrate value for money. ■ Implementation metrics focus on coverage rather than disease averted per US$ 1000 spent.
Quality	Reduction in effectiveness of existing products by insecticide resistance.	■ Limited implementation of GPIRM strategy in the field, due to: ◆ limited choice of products available for use to combat resistance; ◆ lack of on-the-ground expertise and capacity in countries; ◆ the cost–benefit of combating insecticide resistance is not widely understood, resulting in inadequate funding being allocated for implementation.
	Uncertain linkages between LLIN durability, field life and value for money.	■ Durability and effectiveness of any product varies significantly by region, making it difficult to predict durability. ■ Existing strength tests are poor predictors of field performance. ■ Donors are unwilling to purchase "longer lasting" nets at higher prices until performance is fully validated.
Acceptability	Limited uptake of IRS in contrast to LLIN.	■ IRS programmes are complex and costly to implement. ■ Metrics focus on coverage versus disease averted per US$ 1000 spent.

Delivery	Risk that some established LLIN suppliers may exit the market.	■ Innovator companies believe that the focus on lowest cost procurement by concentrated donor buyer groups has driven down prices from suppliers to levels that do not provide returns adequate enough to reward the cost of capital of the R&D-based industry. Current prices paid for nets are only sufficient to sustain generic producers with low overhead and no innovation to reward.
	Difficulty shifting to a consumer-driven market.	■ LLIN market distorted by donor-supplied free nets in mass campaigns.
	Potential significant gaps in coverage in some areas outside of Africa.	■ Current donors have not focused scale-up efforts on populations that have the potential to purchase protection products on their own (i.e. population segments in South-East Asia).

Potential interventions

The potential interventions that have been identified are described in Table 2. This section is not specific to the UNITAID mandate and business model, but rather represents a range of market-based interventions that could be undertaken by different global health actors and stakeholders.

Table 2: Description of potential interventions

Category	Shortcoming	Potential intervention
Availability	Lack of new products and paradigms, particularly to address resistance and durability concerns.	■ Co-fund R&D, particularly in earlier high-risk stages. ■ Provide advanced market commitments sufficient to reward industry investment in R&D for innovations targeted at specified critical areas such as resistance management insecticides suitable for use in LLIN. ■ Consider providing innovators a minimum period of exclusive sales, as done in agricultural markets, in order to allow for return on R&D investment.
	Innovative products face difficulties reaching the market in a timely fashion.	■ Consider changes to WHOPES that may reduce time needed for evaluation and recommendation, including acceptance of industry data, provided they meet certain defined standards. ■ Accept prequalification of the safety and environmental data package of new active ingredients by major regulatory agencies (e.g. Environmental Protection Agency; European Union). ■ Assess if provision of extra funding to increase capacity would improve the speed of evaluation and recommendation. ■ Appoint independent project "guides" to facilitate project progress through WHOPES. ■ Set up online system for VCAG and WHOPES project review consultation, with quarterly meetings of small core groups to make decisions. ■ Consider setting up a fast track country registration for a product with WHOPES recommendation.
Affordability	Higher cost of products for resistance limits uptake.	■ Fund purchase of initial sales to enable: ◆ generation of large-scale use data that demonstrate cost–effectiveness under field conditions to enable purchase by major donors; ◆ building up production and batch scale to improve affordability.

Quality	Degradation of existing products by insecticide resistance.	■ Provide more resources for IRM to support: ◆ development of new products to combat insecticide resistance; ◆ identification where new tools (such as synergists) can be used; ◆ implementation of the Framework for National Insecticide Resistance Plans; ◆ dedicated expert support where needed; ◆ development of cost–benefit models and communications to ensure funding is allocated to IRM.
	Uncertain linkages between LLIN durability and field life value for money.	■ Develop new tests and metrics that more accurately predict field performance and life. ■ Fund studies and/or initial sales of "higher durability" nets to enable generation of large-scale use data that demonstrate cost–effectiveness under field conditions to enable purchase by major donors. ■ Donors purchase nets that provide best lifetime value for money, even if this is at a higher unit price. ■ Educate users on best practice for net use and care.
Acceptability	Limited uptake of IRS in contrast to LLIN.	■ Co-fund IRS in high-transmission areas where LLIN intervention is not effective or where net use levels are poor (e.g. areas where pyrethroid resistance is at high levels of intensity and there is evidence of poor disease control).
Delivery	Risk that some established LLIN suppliers may exit market.	■ Recognition that quality and innovation generates extra costs that require higher prices to reward. Open book accounting can be used to validate profit margin.
	Difficulty shifting to a consumer-driven market.	■ Conduct an analysis to identify where it may be appropriate to encourage the development and sustenance of retail sector by use of voucher schemes to deliver nets in routine distribution programmes. ■ Conduct an analysis to identify where it may be appropriate to fund a pilot programme with subsidized retail sales of LLINs in a market with current retail sales of UTNs.
	Potential significant gaps in coverage in some areas outside of Africa.	■ Fund study to understand extent of coverage, including consumer purchased products.

2 Introduction

This report is part of an initiative within UNITAID to describe and monitor the landscape for malaria commodities. This report focuses on product, technology and market dynamics around malaria vector control products that impact at-risk populations in endemic countries, particularly the primary tools of insecticide-treated nets (ITNs) and indoor residual spraying (IRS). It provides an overview of the current ITN and IRS technology and market landscape, and a high-level perspective on barriers to delivery and access. Information in this report was collected through a variety of methods, including desk research, literature reviews and expert interviews.

This report (along with others) will facilitate informed decision-making by the UNITAID Board, support the Proposal Review Committee should they evaluate any relevant proposals and serve as a global public good for other donors, global health organizations and malaria programmes.

The report is structured as follows:

- Section 3 provides an overview of the vector control approaches and the global trends in coverage and use.
- Section 4 is an overview of the technology landscapes for the main categories of interventions: insecticides, IRS, ITNs and long-lasting insecticidal nets (LLINs), discussing the range of products available as well as those products currently in the research and development (R&D) pipeline.
- Section 5 provides an overview of the market landscape for the main categories of interventions (insecticides, IRS and ITNs/LLINs), discussing supply and demand market characteristics.
- Section 6 summarizes the critical near-term and long-term challenges in the malaria vector control market, and gives an overview of the major market shortcomings and their causes.
- Section 7 discusses possible market interventions that could address the market deficiencies.

Methodology

In order to gather a comprehensive view of malaria vector control commodity issues, several sources of data were used. Desk research identified public information available on vector control products, specifically insecticides, nets and IRS. Examples include: the World Malaria Report 2013; the Global Plan for Insecticide Resistance Management (GPIRM) in malaria vectors; and the Global Malaria Action Plan (GMAP).

A number of interviews were conducted with malaria experts from various international stakeholders, including the World Health Organization (WHO), the Roll Back Malaria Partnership (RBM), the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), the United States President's Malaria Initiative (PMI), the Innovative Vector Control Consortium (IVCC) and industry suppliers.

Data were primarily collected during the period from May 2014 to September 2014.

Caveat: This document consolidates data from different sources and different periods. Since no information is available on the overall malaria vector control commodities market, we have, therefore, extrapolated from these sources to draw general conclusions about the global market. For this reason, data sets from different analyses might not be immediately comparable with each other. In addition, given the limited amount of robust data available on the malaria vector control market, it is important to note that individual countries may vary from the picture described here.

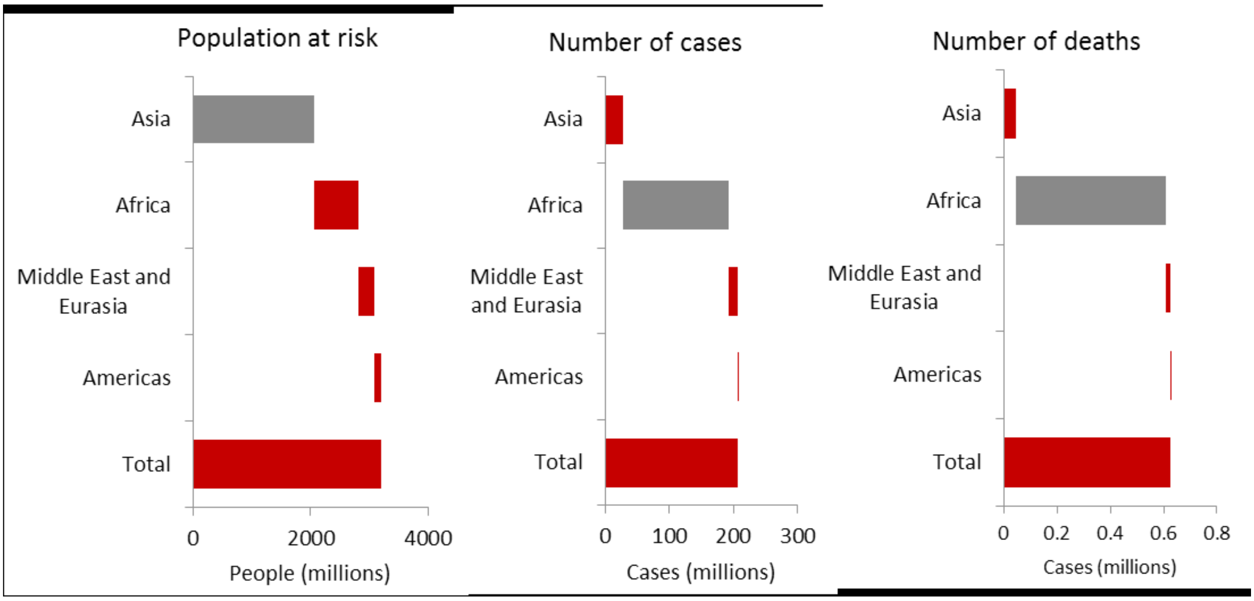
3 Malaria today

3.1 Disease overview

Malaria is a vector-borne parasitic disease caused by the parasite *Plasmodium* and spread through the bite of *Anopheles* mosquitoes. Though prevention and drug treatment exist, symptoms of severe chills, headaches and high fever can ultimately progress to coma and death if the disease goes undiagnosed and unaddressed. Malaria mortality primarily impacts children, with 85% of cases in children under 5 years old [1].

Malaria is a global challenge. In 2012, WHO estimated the global population at risk for malaria to be 3.2 billion people [1]. While 2.1 billion of the at-risk population resided in Asia, Africa represented 80% of the worldwide cases and 89% of the deaths (Figure 1). Since 84% of the at-risk population in Asia lives in areas of low transmission, the region has a low malaria burden given its large size. Africa is often the focus of malaria discussions because of the disproportionally high burden for the 800 million at-risk people, or 24% of the global at-risk population, living in the region. In 2012, the Americas, Eurasia, Europe and the Middle East accounted for approximately 12% of the global at-risk population and contributed minimally to global cases and deaths [1].

Figure 1: Malaria at-risk population, cases and deaths by region in 2012 [1]

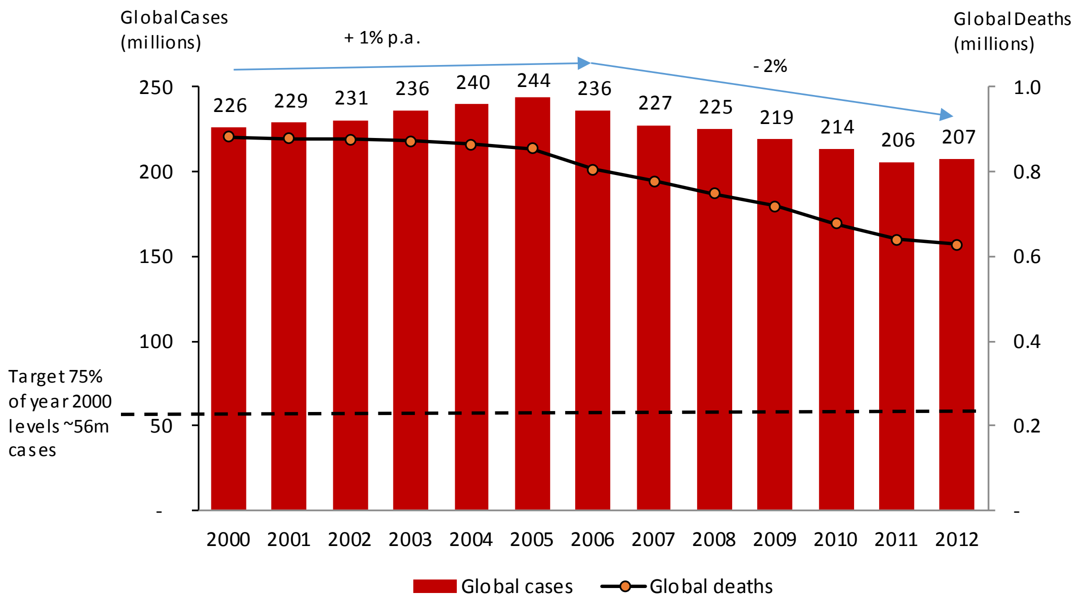


The global health community has set forth various goals for the control and eventual eradication of malaria. In a 2007 resolution (WHA58.2), the World Health Assembly (WHA) targeted a 75% global malaria burden reduction from 2000 levels by 2015, or a reduction of 167 million cases, as part of achieving the

United Nations (UN) Millennium Development Goals; similarly, RBM has targeted a goal of near-zero preventable deaths by 2015 [2]. In addition, malaria is a key priority on the UN Secretary-General Five-year Action Agenda for 2012–2017.

To date, much progress has been made in addressing malaria in various regions as awareness and funding has increased efforts to scale up prevention and treatment. Released in 2008, GMAP helped focus the malaria community on the long-term goal of eradication [3]. However, malaria still represents a major global health issue today. The number of cases worldwide has decreased only 8% since 2000 to 207 million cases in 2012, far from the 75% reduction targeted. There was a slight increase in the overall number of cases in 2012. Similarly, the number of deaths caused by malaria has decreased 29% since 2000 to 627 000 deaths in 2012 (Figure 2) [1]. While the overall global gains in malaria control have been modest, the World Malaria Report 2013 stated that approximately 52 of the 103 countries with ongoing malaria transmission are on track to hit the target of reducing malaria case incidence by 75% by 2015.

Figure 2: Global malaria cases and deaths, 2000–2012



3.2 Vector control overview

Vector control is one of the primary tools used for preventing malaria as part of broader control and elimination efforts. Vector control also can be used to control additional vector-borne neglected tropical diseases, mainly dengue and leishmaniasis.

Vector control goals

The global health community has established specific goals for vector control as part of the broader objectives in controlling malaria, as discussed earlier. In prior years, coverage goals had been targeted primarily at those most at risk for malaria—pregnant women and children under 5 years old. Specifically, the goal previously was to reach 80% coverage of children and pregnant women by 2010, and 100% coverage by 2015. WHO and RBM have expanded these targets to strive for broader, universal (100%) coverage of the global at-risk population by 2015. Beyond 2015, the goal is to sustain universal coverage for all populations at risk until local field research suggests that coverage can gradually be targeted to high-risk areas and seasons only, without the risk of a generalized resurgence [3].

Interventions

There is a range of different vector control approaches (Table 3). WHO primarily recommends use of the WHO Pesticide Evaluation Scheme (WHOPES)-recommended LLINs and IRS for malaria control as they are the most effective at reducing the mosquito population and their ability to transmit (through reduced lifespan). There is limited endorsement of larviciding, space spraying and environmental management and only in specific contexts.

Table 3: Summary of vector control interventions

Approach	Description	Insecticide (if applicable)
Bednets	UTNs: A net material that acts as a physical barrier between a person and mosquitoes, inhibiting blood feeding and, therefore, transmission.	Not applicable
	ITN: A mosquito net that also can inhibit blood feeding and kills mosquitoes coming into contact with netting fibres coated with insecticide by dipping the net in a solution of insecticide and water. The insecticide treatment can provide from 6 to 12 months of protective effect, depending on washing mode and community practices and thus requires periodic re-treatment.	Pyrethroids and pyrethroids with synergists only
	LLIN (or LN): Insecticide is incorporated within or bound around the net fabric. WHO defines an LLIN as a factory-treated net expected to retain its biological activity for at least 20 standard washes under laboratory conditions and three years of recommended use under field conditions.	
IRS	Application of chemical insecticides on interior walls and roofs of all houses in a given area, killing vectors that rest on those surfaces. Spraying domestic animal shelters also is done in some countries.	Pyrethroids Organochlorines (DDT) Organophosphates Carbamates
Larviciding	Reduces vector population growth by identifying larval habitats and acting on them to reduce mosquito larvae by means of either chemical insecticides or biological tools. WHO does not recommend this approach for malaria control except where breeding sites are "few, fixed and findable" and only in conjunction with LLIN or IRS use.	Organophosphates Carbamates Insect growth regulators (IGRs) and spinosyns as chemicals Bacteria and fish as biological tools
Space spraying	Consists of the dispersion into the air of a diluted insecticide, effective at killing vectors that come in contact with the insecticide while airborne. Space spraying has been used for other vector-borne diseases such as dengue, but is recommended only in extreme circumstances for malaria control such as epidemics in urban areas or refugee camps.	Pyrethroids Organophosphates
Environmental management	Consists of the modification or manipulation of environmental factors to reduce vector breeding, mainly acting on water accumulation sites. May also include house screening to prevent entry of mosquitoes.	Not applicable

Approach	Description	Insecticide (if applicable)
Other products	Consumer products (household insecticides): Products primarily available through the private sector market and used for nuisance abatement. Examples: coils, vaporizing mats and aerosols that incorporate an insecticide or repellent; lotions and wipes are also common.	Pyrethroids Carbamates Plants and oils with repellent effect
	Wall linings: Treated wall linings are a potential alternative to IRS. For example, a lining of loosely woven high-density polyethylene panels treated with insecticide could be installed on the walls of a house. Wall linings may also address some issues of consumer acceptance as they may be perceived as enhancing the interior style of walls. Wall linings are not currently recommended by WHO.	Pyrethroids

The most appropriate intervention is based on the specific conditions under which it is going to be implemented and, therefore, can vary due to infrastructure, vector ecology and environmental constraints, transmission levels, implementation capacity, cultural habits and acceptance and, ultimately, available funding. Nets followed by IRS are the primary forms of vector control in use due to the ease of scale-up and use and the clear evidence of impact, particularly on vectorial capacity. As a result, universal coverage has commonly focused on 100% coverage of nets or IRS in a given country or district.

Untreated nets (UTNs) may represent a substantial portion of the overall market beyond the demand and coverage discussed in this report; however, the UTN segment of the overall preventatives market is not a focus of this landscape. In 2005, a study of a small region in Mali showed 98% coverage of bednets (all forms), but 11% coverage of ITNs. Similar levels of coverage were documented in Cambodia during this time. Additional data are needed to understand how education and mass campaign efforts, as well as the introduction of LLINs, have impacted the relative proportion of untreated versus treated nets.

The remainder of this report concentrates on insecticides and the insecticide-based interventions—ITNs, LLINS and IRS.

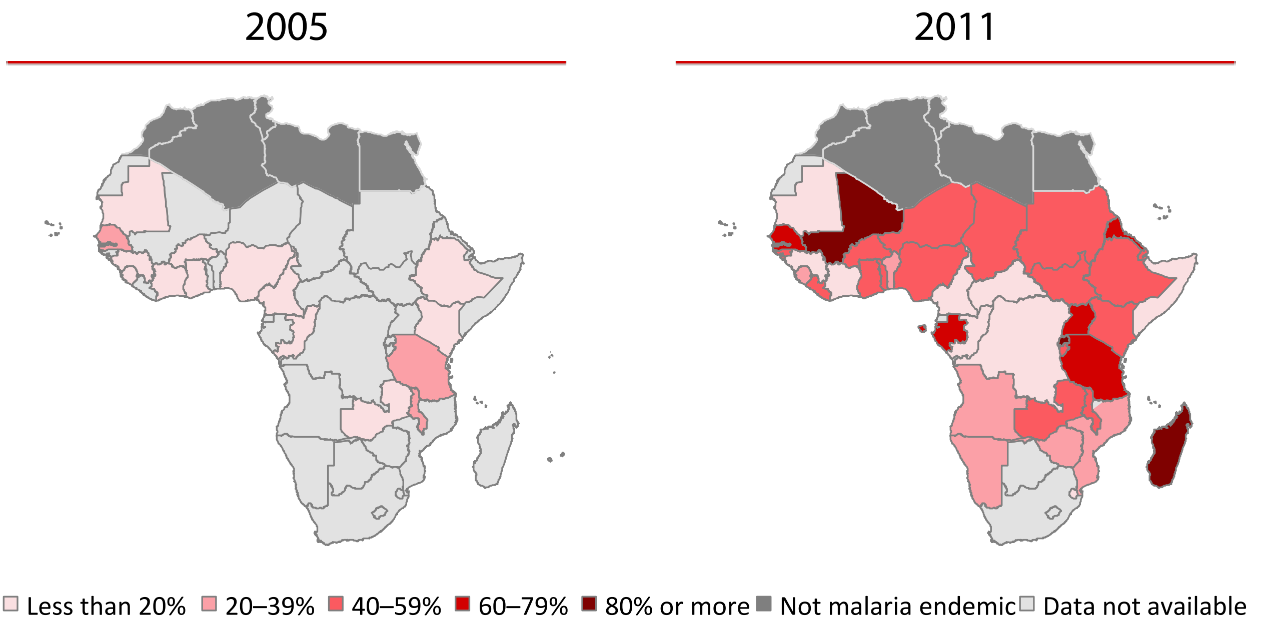
3.3 Global trends

Over the past five years, there has been significant progress in the scale-up of nets and IRS globally. Based on data from the World Malaria Report 2013, 380 million ITNs/LLINs are estimated to be in use, protecting around 20% of the 3.2 billion people globally at risk, and 136 million people were protected by IRS [1]. However, commodity access issues remain and have limited the ability to meet universal coverage targets.

ITN use and IRS coverage have increased substantially over the last five years, driven in part by the decreasing average cost of LLINs, which has fallen over the past decade to around US$ 3.00 [4]. Between 2011 and 2013, around 80% of the global LLIN deliveries were concentrated in sub-Saharan Africa. Africa has experienced a substantial increase in LLIN coverage between 2005 and 2011 (Figure 3).

Both 2009 and 2010 were years of substantial scale-up of vector control interventions globally, primarily of bednets. Deliveries fell back in 2011 and 2012 but picked up again in 2013 and 2014 and reached the required level to replace those that had reached the end of their three-year lifespan and maintain coverage—around 165 million. While many households have at least one net, the current recommendation is for one net per approximately two people, indicating that many households will require more than one net to cover the entire house.

Figure 3: Proportion of households with at least one ITN



Note: Based on the latest survey available in the respective years up to 2011. Subsequent surveys have shown that coverage has increased in the United Republic of Tanzania (91%), Côte d'Ivoire, (67%) and the Congo (33%), but decreased in Gabon (36%).

Source: World malaria report 2011. Geneva: WHO; 2012.

ITNs have proven to be highly effective tools for controlling malaria, especially when used at high coverage rates. When high community coverage is achieved, the overall number of mosquitoes, as well as their individual lifespan, will be reduced. When this happens, all community members have some level of protection regardless whether or not they use a net. In areas with high coverage rates, bednets can reduce malaria cases by 40–60% [3].

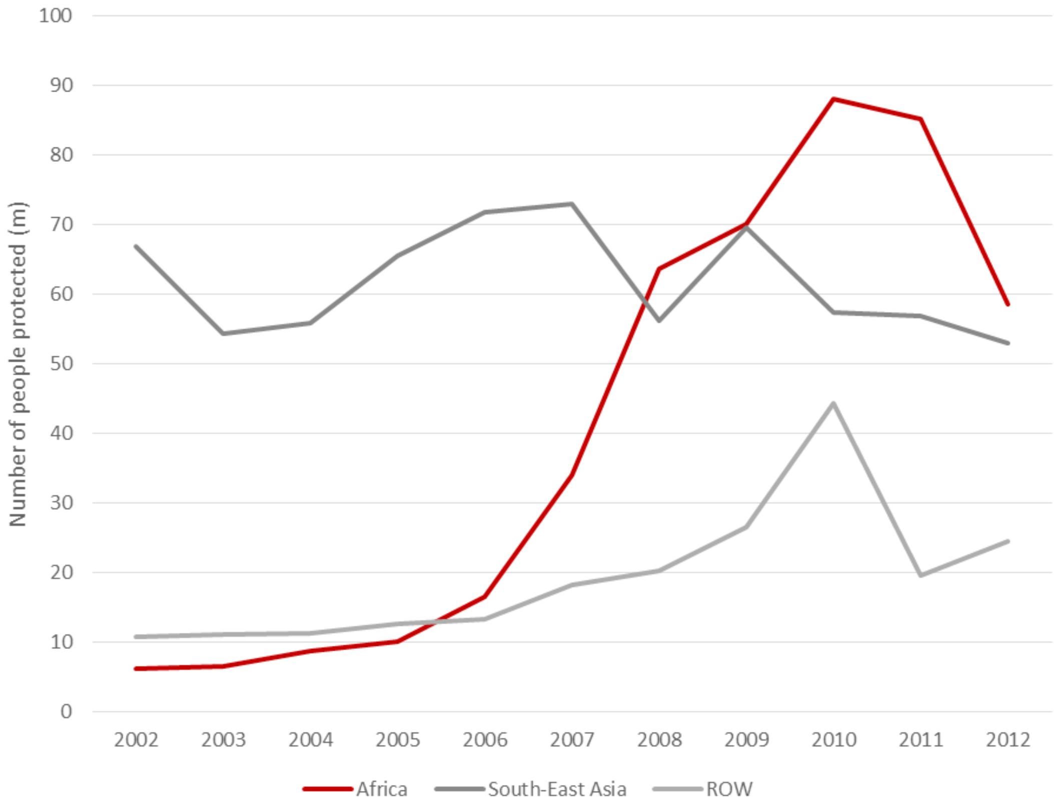
Outside of Africa, nine countries account for 70% of the total 79 million nets in use: India 18.4 million; Indonesia 7.7 million; Afghanistan 6.1 million; Myanmar 5.5 million; Papua New Guinea 4.2 million, Cambodia 4.1 million, Philippines 3.9 million; Nepal 3.3 million and Haiti 3.1 million.[1]

Current coverage rates vary dramatically by region, country and district. Coverage variations are attributable to many geographical differences such as transmission rates, disease burden, governmental infrastructure and historical coverage targets. For instance, in Africa, where 81% of the at-risk population lives in areas of high transmission, all countries in the control stage use LLINs. Similarly, in Eurasia and the Middle East, LLINs are the main form of vector control. On the other hand, both the Americas and Asia have significantly different LLIN usage. In the Americas, only six countries target the entire at-risk population with LLINs, and although Asia represents 65% of the global at-risk population, coverage with donor-funded LLINs has been historically low. In the Americas and Asia, IRS has historically been the predominant prevention tool [3].

IRS coverage also has increased since 2005, although it has shown some decline since 2011. Historically, global IRS efforts have been poorly monitored and tracked, resulting in minimal and poor data on coverage rates, prices, manufacturers and suppliers. Between 2006 and 2008, two community events prompted major increases in IRS coverage of the at-risk populations in Africa and the Americas (Figure 4): the global call-to-action to prevent malaria transmission and the establishment of PMI, which focused on curbing malaria primarily in Africa through IRS and other interventions [5]. Other regions have seen only slight fluctuations. There has been a fall-off in coverage of IRS in Africa since 2011, due to the need to use higher cost insecticide products to address insecticide resistance.

1 Based on nets delivered to markets in the period 2011–2013. Data from Milliner Global Associates, Net Mapping Project, personal communication, July 2014.

Figure 4: IRS use by region



Sources: World Malaria Report 2013. Geneva: WHO; 2014. NMCP reports.
ROW = rest of world (including the Americas)

4 Technology landscape

4.1 Technology landscape: insecticides

Currently, four classes of insecticides are used and recommended by WHOPES for use in IRS and one in LLINs, which are the primary intervention methods for malaria vector control (Table 4).

Table 4: Characteristics of the four classes of insecticide currently recommended by WHOPES for malaria vector control for use in bednets and IRS [6]

Insecticide class	Molecules available	Advantages	Limitations	Duration of IRS effect
Pyrethroids	■ Alpha-cypermethrin ■ Bifenthrin ■ Cyfluthrin ■ Deltamethrin[2] ■ Lambdacyhalothrin ■ Etofenprox ■ Permethrin[2]	■ Low toxicity to humans ■ Rapid knock-down effect[1] ■ *Deltamethrin CS formulation has a 6-month duration of effect	■ Resistance developed in many countries	3–6 months*
Organo-chlorines	■ DDT	■ Rapid knock-down effect[1] ■ Relatively long residual activity ■ Historically low cost, although scarcity may be driving cost up	■ Banned in agriculture due to concerns about long-term toxicity effects ■ Possible cross-resistance with pyrethroids, due to similar modes of action	>6 months
Organo-phosphates	■ Fenitrothion[3] ■ Malathion[3] ■ Pirimiphos-methyl	■ Wide range of chemicals in this class ■ Considered highly effective, results in neuromuscular overstimulation ■ *Pirimiphos-methyl CS formulation has a 4–6 month duration of effect	■ Short residual activity ■ High cost ■ Toxicological monitoring recommended, especially for spraying operators ■ Mode of action similar to carbamates, with possible cross-resistance	2–6 months*
Carbamates	■ Bendiocarb ■ Propoxur[3]	■ High effectiveness	■ Short residual activity ■ High cost ■ Mode of action similar to organophosphates, with possible cross-resistance	2–6 months

1 Reference knock-down time is usually the time it takes for 50% and 95% of the mosquitoes to die. There is wide variation, mainly depending on insecticide resistance status, but the lowest times for 50% mortality are 8–10 minutes for DDT.

2 Some nets with these active ingredients also include the synergist piperonyl butoxide.

3 PMI and IVCC report that there is either very limited or no availability of fenitrothion, malathion and propoxur.

*Report of the 16th WHOPES Working Group Meeting, WHO, Geneva, July 2013.

WHOPES also recommends a range of insecticides for control of mosquito larvae. This includes four additional insecticide classes (Table 5) [7].

Table 5: Insecticides recommended for larviciding

Insecticide class	Compounds available
Bacterial larvicide	■ Bacillus thuringiensis (var. Israelensis)
Benzoylurea (insect growth regulator)	■ Diflubenzuron
Juvenile hormone mimic (insect growth regulator)	■ Pyriproxyfen
Organophosphate	■ Chlorpyrifos ■ Fenitrothion ■ Pirimiphos-methyl ■ Temephos
Spinosyns	■ Spinosad

Note: WHO recommends use of larviciding only as an addition to the use of LLIN or IRS and in situations where mosquito breeding sites are "few, fixed and findable" [8].

Certain pyrethroid, carbamate and organophosphate insecticides are also recommended by WHOPES for space spraying.

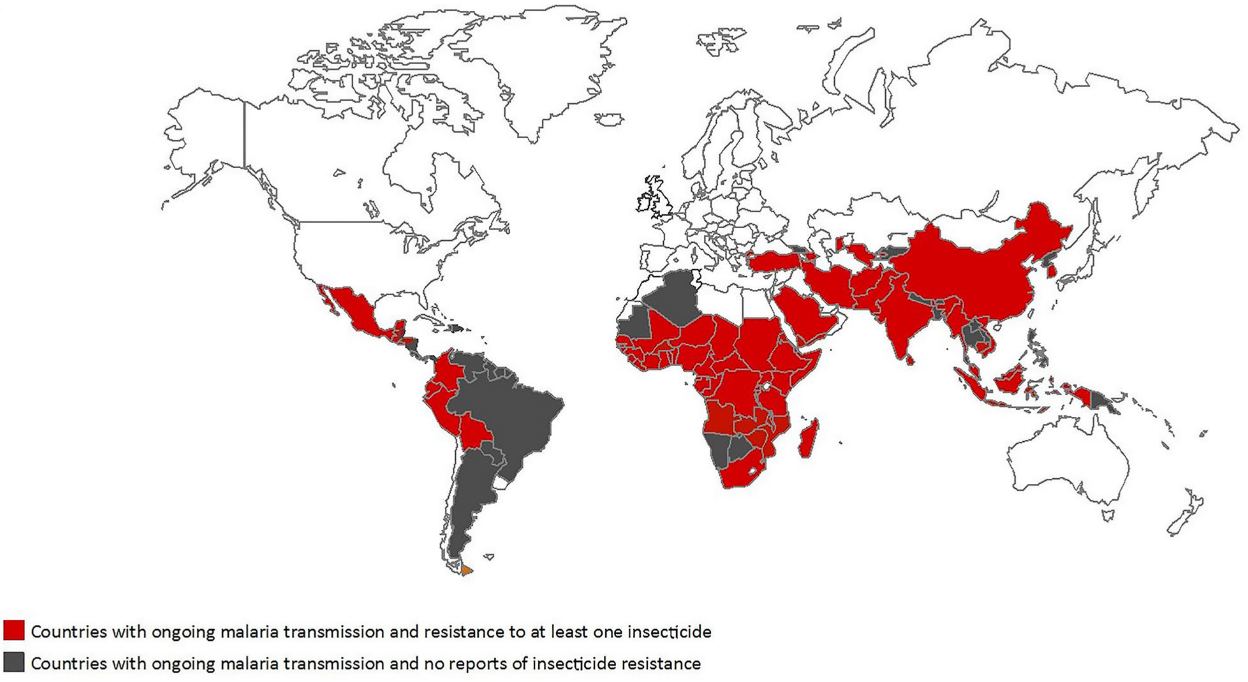
Insecticide resistance

Insecticide resistance is a major issue for malaria vector control and presents a serious risk to the effectiveness of existing insecticide-based tools. Unless new tools become available soon, there is a real risk that the gains in malaria control made over the last decade will be lost within a few years.

The limited number of insecticide classes that are available is a challenge for effective insecticide resistance management (IRM), particularly as the mechanisms of action are similar between pyrethroids and organochlorines and between organophosphates and carbamates.

Resistance has been detected in *Anopheles* mosquitoes against all of the four major classes of insecticide and at least one class of insecticide resistance has been found in over 64 countries (Figure 5). Resistance to pyrethroids, which are by far the most widely applied class of chemicals currently used in vector control, appears to be widespread and rapidly developing in intensity.

Figure 5: Countries reporting insecticide resistance [6]



The impact of resistance on control of malaria is difficult to quantify. South Africa, in 2000, has been the only broadly accepted case of control failure due to metabolic resistance to pyrethroids used in an IRS programme [6]. However, there is growing anecdotal evidence from the field in some countries in Africa that LLINs are becoming less effective in preventing mosquitoes from blood feeding, suggesting the effectiveness of LLINs in some situations may be reduced to acting as only a physical barrier.[2] The impact of resistance to malaria control has also been seen in situations where switches have been made from using pyrethroid IRS to organophosphate or carbamate IRS. Recent data from an area of Ghana where there had been regular use of pyrethroid IRS for three years, showed that after a switch to using a long-lasting organophosphate for IRS, the levels of malaria parasitaemia fell by 56%,[3] suggesting the pyrethroid IRS programmes were not optimally controlling transmission. A trial in Sudan during 2013 found a substantial reduction in malaria incidence following a switch from pyrethroid IRS programmes to a bendiocarb (carbamate) programme.[4]

GPIRM was published in 2012 [6], and sets out technical strategies to manage insecticide resistance with the aim of preserving the effectiveness of insecticides used in vector control. In summary, the strategy laid out in GPIRM is a five-pronged approach, including: (i) planning and implementing IRM strategies in endemic countries; (ii) ensuring proper, timely entomological and resistance monitoring and effective data management; (iii) developing new and innovative vector control tools; (iv) filling in gaps in knowledge; and (v) ensuring that enabling mechanisms are in place. Since many of these strategies represent an increase in cost, many funders and implementing countries will be faced with short-term tradeoffs in managing resistance versus achieving and sustaining high levels of coverage.

In the two years since the launch of GPIRM the insecticide resistance situation has worsened significantly, particularly in the African Region. Pyrethroid resistance has continued to spread in the major African malaria vectors of *Anopheles gambiae* and *Anopheles funestus*. New resistance mechanisms have been detected in *An. gambiae* from West Africa in addition to those formerly circulating. This has resulted in levels of resistance elevated by an order of magnitude as well as cross-resistance to additional insecticides.[5]

There has been very limited progress in implementation of the plan to date at the country level. GPIRM calls for monitoring of insecticide resistance patterns and annual rotation of two different classes of insecticide. WHO is in the process of rolling out a generic template for use at the country level. While most countries have implemented some form of monitoring and some have moved away from pyrethroid-based IRS, the challenges of cross-resistance and limited availability of alternative products means that no country has yet succeeded in implementing a rotation plan completely consistent with the GPIRM recommendation. Among other reasons, it is believed that limited progress is related to a lack of expert capacity on the ground and to funding constraints[6] [9]. In addition, it is difficult for governments and donors to easily calculate the value of IRM activities.

The widespread and growing risk posed by resistance is the major driver behind efforts to find and introduce new classes of insecticides not already used in vector control.

4.2 Technology landscape: ITNs and LLINs

Description and policy on use

An ITN is a mosquito net that primarily kills mosquitoes coming into contact with the insecticide on the netting material and inhibits blood feeding. Nets are placed inside houses or huts, hung above beds with a hook or hooks, and have become one of the major vector control interventions due to their high cost–effectiveness and ease of scale-up.

2 Janet Hemingway, Liverpool School of Tropical Medicine, personal communication, 31 July 2014.
3 Kristen George. PMI Indoor Residual Spraying Programme. Presentation at the Global Fund IRS Supplier Conference, Geneva, April 2014.
4 WHO, Update on GPIRM implementation, August 2013, unpublished.
5 WHO, Update on GPIRM implementation, August 2014, unpublished.
6 Janet Hemingway, Liverpool School of Tropical Medicine, personal communication, 31 July 2014.

Bednets fall into three main categories: UTNs; ITNs (treated nets usually dipped in insecticide mixed with water and requiring re-treatment approximately every six months); and LLINs (insecticide impregnated into or coated onto the fibres, usually lasting about three years).

Treated nets are effective in three ways: (i) acting as a physical barrier to prevent mosquitoes from biting individuals while sleeping; (ii) repelling mosquitoes; and (iii) killing mosquitoes after coming in direct contact with the insecticides present on the net. In addition, a community effect occurs above a certain level of coverage due to an overall reduction in transmission and, therefore, reduced risk of contact with an infected mosquito, indirectly protecting those not sleeping under the net.

ITNs were developed in the 1980s, and LLINs were developed and introduced to the market about a decade later in the late-1990s. LLINs have a clear advantage over ITNs due to a much longer residual efficacy, thus eliminating the need to re-treat every six months. While LLINs have replaced ITNs in most countries, ITNs are still available in certain retail markets, particularly in Asia. Donors almost exclusively fund LLINs over ITNs.

As noted earlier, WHO recommends universal coverage of all people at risk for malaria with LLINs, expanding beyond initial recommendations only for children under 5 years old and pregnant women. Furthermore, WHO recommends use of LLINs at ideally one net per two people. With an average household size of about four to five members, this would mean two or three nets per household although the WHO metric currently being tracked is at least one net per household [10].

As of August 2014, WHOPES recommends the use of 11 LLINs (Table 6).

Table 6: LLINs recommended for use by WHOPES as of August 2014 [11]

LLIN recommended	Supplier	Status of WHO recommendation	Product type
DawaPlus® 2.0	Tana Netting (NRS), Dubai	Interim	Deltamethrin coated on polyester
Duranet®	Shobikaa Impex, India Bestnet, Denmark	Full	Alpha-cypermethrin incorporated into polyethylene
Interceptor®	BASF, Germany	Full	Alpha-cypermethrin coated on polyester
LifeNet®	Bayer, Germany	Interim	Deltamethrin incorporated into polypropylene
*MAGNet™	V.K.A. Polymers, India	Full	Alpha-cypermethrin incorporated into polyethylene
Olyset®	Sumitomo Chemical Co., Japan Net Health, United Republic of Tanzania AtoZ, United Republic of Tanzania	Full	Permethrin incorporated into polyethylene
OlysetPlus®	Sumitomo Chemical Co.	Interim	Permethrin and piperonylbutoxide incorporated into polyethylene
PermaNet® 2.0	Vestergaard Frandsen, Switzerland	Full	Deltamethrin coated on polyester
PermaNet® 3.0		Interim	Combination of deltamethrin coated on polyester with strengthened border (side panels) and deltamethrin and piperonylbutoxide incorporated into polyethylene (roof)
*Royal Sentry®	Disease Control Technologies, India	Full	Alpha-cypermethrin incorporated into polyethylene
*Yorkool LN®	Tianjin Yorkool International Trading Co., China	Full	Deltamethrin coated on polyester

* Recommendations based on equivalency

Currently, all of the LLIN products use insecticides from the pyrethroid class. Pyrethroids are ideally suited for use in nets due to their high activity, good persistence and favourable toxicity and physical chemical properties, but the reliance on a single class of insecticide is a major risk due to the increasing spread and intensity of insecticide resistance in the field. Nets containing additional chemicals that act as synergists and reduce the effect of certain pyrethroid resistance mechanisms in mosquitoes are now available and have recently been supported by the Vector Control Advisory Group (VCAG) [12]. Since the synergists are more effective against some resistance mechanisms than others and are most effective before resistance is present at very high levels, a significant challenge remains in deciding which geographical areas are most suitable for their deployment.

Equivalency-based recommendation for generic nets

WHOPES follows an Equivalency Process that allows new LLIN products to receive WHOPES recommendation status (interim or full) based on their laboratory efficacy and wash resistance (Phase 1) and chemical equivalency to the innovator LLIN product. These "comparator" products are granted WHOPES interim or full recommendation status based on results from WHOPES Phase 1 testing and full compliance with WHO specification of the originator LLIN using independent GLP physico-chemical data. By contrast, to achieve interim recommendation status, an innovator LLIN must have passed both Phase 1 and 2 testing, and to achieve full recommendation, it must have passed Phase 1, 2 and 3 testing. There are three comparator LLIN products that currently have interim or full status based on their equivalency to innovator products that hold those statuses. These products are marked with an asterisk (*) in Table 6.

PMI, a major donor of LLINs, has decided that the equivalency status based on Phase 1 laboratory studies is insufficient to determine eligibility for PMI procurement because, in the view of PMI, these studies do not determine how the LLIN product functions in the field where other factors come into play, particularly physical durability and long-term bio-efficacy [13]. PMI policy does not currently allow for procurement of the comparator nets unless Phase 2 testing has been completed. Currently, the other the major LLIN donors, GFTAM and the United Nations Children's Fund (UNICEF), accept procurement of nets based on the Equivalency Process.

LLIN durability and net life in the field

Studies have shown that around 50% of the protective effect of an LLIN comes from the physical barrier to feeding [14]. If a net becomes worn or has holes and allows mosquitoes to reach users under the net, the level of protection provided is, therefore, significantly reduced. Useful field net life is also a key driver of lifetime use cost and thus an important consideration in value for money procurement.

A core assumption in LLIN programmes is that the nets can have a useful life in the field of around three years. Field observations suggest actual net life may be significantly shorter or longer, with the variations due to the interaction of external use conditions (e.g. storage on the ground versus being hung up when not in use during the day; frequency of washing) with net materials and design.[7] The evidence for comparative performance of different nets in the field has been limited and based mostly on anecdotal observations. However, PMI-supported studies comparing the field performance of different net brands highlighted significant differences between them and led to one manufacturer changing the weave design to improve performance.[8] The WHOPES system has some basic tests to ensure that all nets meet a minimum measure of strength, but these tests have limited capability to predict field durability.[6]

A recent in-depth study has analysed the causes for net failure in the field across multiple continents and countries. Based on this, a series of laboratory tests was identified that replicates this damage, allowing a determination of the strength of nets and their resistance to damage against common threats in the field. The study proposes that data from the tests could be used to help purchasers improve value for money in purchasing by allowing them to value nets on the basis of both price and performance, while helping manufacturers improve net materials and designs to improve net durability and life.[9] In addition, WHO and

7 Albert Kilian, Tropical Health LLP, personal communication, 23 July 2014.
8 Christen Fornadel, PMI, personal communication, 31 October 2014.
9 Kanika Bahl, Results for Development Institute (R4D), personal communication, 12 August 2014.

the Global Fund have worked together on a study of laboratory measures for LLIN fabric strength. Based on this, recommendations on methods and strategies for monitoring and assessing LLIN fabric strength in the laboratory and the field have been made. At the time of writing, these have not been published.[10]

4.3 Technology landscape: IRS

Description and policy on use

IRS is the organized spraying of an insecticide on the inside walls of houses prior to peak malaria transmission. It is designed to interrupt malaria transmission by either killing adult female mosquitoes when they enter houses or when they rest on the walls after feeding [15]. Some insecticides, such as pyrethroids, may also have a repellent effect, deterring entry or settling in a dwelling, but this effect is considered to be relatively small [15]. Indoor spraying has helped to greatly reduce or eliminate malaria from many areas of the world, particularly where the mosquito vectors feed and rest indoors and where malaria is seasonally transmitted [15]. An important strength of IRS, when it has been properly applied, is that it is less dependent on user behaviour than LLINs (e.g. people not using nets) to provide protection from indoor transmission.

IRS is recommended for use by WHO [15] where:

- the majority of the vector population feeds and rests inside houses;
- vectors are susceptible to the insecticide in use;
- people mainly sleep indoors at night;
- the malaria transmission pattern is such that the population can be protected by one or two rounds of IRS per year (economics often mean only one campaign is used per year);
- the majority of structures are suitable for spraying;
- structures are not scattered over a wide area, resulting in high transportation costs.

There are four WHO-recommended classes of insecticide: pyrethroids; organophosphates; organochlorines; and carbamates. Until recently, pyrethroids were the most commonly used class due to their long persistence and low cost. The rapid spread and intensification of pyrethroid resistance and widespread use of pyrethroids in LLINs is now driving use to other insecticide classes such as carbamates and organophosphates for IRS use.

It is important that IRS products have long persistence that can provide protection throughout the peak transmission period so that multiple re-applications, which are costly, are not needed. Recent studies from West Africa have shown that IRS applications that have long persistence can provide improved suppression of malaria transmission compared to repeated application of short persistence products.[11] New long lasting-formulations (at least six months or more activity) of the organophosphate insecticide pirimiphos-methyl and the pyrethroid deltamethrin were recommended by WHOPES in July 2013 [16].

10 Raman Velayudhan, WHOPES, personal communication, 4 November 2014.

11 IVCC, personal communication, June 2014.

The current list of WHOPES-recommended IRS products [17] is shown in Table 7.

Table 7: WHOPES-recommended IRS products

IRS recommended	Class	Formulation	Duration (months)
DDT	Organochlorine	WP	>6
Malathion*	Organophosphate	WP	2–3
Fenitrothion*	Organophosphate	WP	3–6
Pirimiphos-methyl	Organophosphate	WP, EC	2–3
Pirimiphos-methyl	Organophosphate	CS	4–6
Bendiocarb	Carbamate	WP	2–6
Propoxur*	Carbamate	WP	3–6
Alpha-cypermethrin	Pyrethroid	WP, SC	4–6
Bifenthrin	Pyrethroid	WP	3–6
Cyfluthrin	Pyrethroid	WP	3–6
Deltamethrin	Pyrethroid	WP, WG	3–6
Deltamethrin	Pyrethroid	SC-PE	6
Etofenprox	Pyrethroid	WP	3–6
Lambda-cyhalothrin	Pyrethroid	WP, CS	3–6

*PMI and IVCC report that there is either very limited or no availability of fenitrothion, malathion and propoxur.
CS = capsule suspension; EC = emulsifiable concentrate; PE = polymer-enhanced; SC = suspension concentrate; WG = water dispersible granule; WP = wettable powder

WHO has recently provided guidance on combining IRS and LLIN deployment [18]:

- In settings where there is high coverage with LLINs and they remain effective, IRS may have limited utility in reducing malaria morbidity and mortality. However, IRS may be implemented in areas where there are LLINs as part of an insecticide-resistance management strategy.
- If LLINs and IRS are to be deployed together in the same geographical location, the IRS should use non-pyrethroid insecticides.
- Malaria control and elimination programmes should prioritize delivering either LLINs or IRS at high coverage and to a high standard rather than introducing the second intervention as a means of compensating for deficiencies in the implementation of the first.

Governments (e.g. ministries of health) are typically responsible for IRS operations, while nongovernmental organizations (NGOs) and other agents generally participate as implementers and supporters.

IRS is delivered during campaigns that require careful planning. Based on entomological studies and bioassays, first the insecticide to be used has to be selected, and then both the insecticide and equipment must be secured. In order to make IRS an effective vector control measure, it is important to perform it with proficiency. The spray operators, who are often new for each campaign, need training sessions that often last about one week. In many cases, training of trainers is also needed. Training and appropriate oversight are critical to ensure the quality and, therefore, the effectiveness of spray operations.

IRS is normally done using hand-operated compression sprayers. Commonly used suppliers include Goizper, H.D. Hudson, Semco Co., Golden Agin, Solo, B&G Equipment Company and Micron. The operators also need protective equipment, including at a minimum goggles or an eye mask, a face mask, long-sleeve overalls, boots, rubber gloves and a hat or helmet due to the health and safety risks of concentrated insecticide exposure. Insecticide spray application equipment is no longer tested by WHOPES for compliance with their WHO specifications; however, WHOPES updates these specifications from time to time. The most recent specification guidelines were published in 2010. The quality of pesticide application equipment can be tested through the WHOPES collaborating centre designated for this purpose: International Pesticide Application Research Centre (IPARC), Ascot, United Kingdom. Meanwhile, WHO is developing guidelines for personal protective equipment.

The insecticide is available in liquid form or soluble sachets, tablets and granules. Depending on the form, the insecticide can be poured directly into the spray tank or has to be previously mixed in a separate container.

During the actual spraying operations, all household items must be removed and furniture must be removed or covered. The occupants must wait until the insecticide is dry, which can take up to two hours. The process causes significant inconvenience for the population, which can lead to opposition from the recipients. In addition, there are many protocols in order to avoid environmental problems; the remaining insecticide and empty packaging after spraying must either be burnt or placed in pit latrines, if available, or into pits that have been dug in the ground.

A critical success factor for IRS is that spraying is carried out to a high quality, with complete coverage and correct dosage of a surface. A simple to use Insecticide Quantification Kit (IQK) is being developed by IVCC to assist programme managers in monitoring the quality of spraying [19].

4.4 Technology landscape: larval source management

Description and policy on use

Larval source management is the management of aquatic habitats (water bodies) that are potential larval habitats for mosquitoes in order to prevent the completion of development of the immature stages. There are four types of larval source management [20]:

1. Habitat modification: a permanent alteration to the environment, e.g. land reclamation.
2. Habitat manipulation: a recurrent activity, e.g. flushing of streams.
3. Larviciding: the regular application of biological or chemical insecticides to water bodies.
4. Biological control: the introduction of natural predators into water bodies.

Larval source management was an important method of malaria control until the 1950s and was successfully used in Brazil, Egypt and Panama. After the introduction of IRS with DDT and then the growth of ITNs, its use declined. There is now renewed interest in larval source management and its practical application in Africa as a complementary intervention to LLINs and IRS, especially where outdoor biting by malaria vectors is problematic or where there is resistance to the insecticides used for LLINs or IRS. However, trials in Africa have shown that larval source management is not effective in all ecosystems [20] and its use needs to be carefully focused and planned.

WHO has provided specific guidance on use of larvicides for malaria control [8], recommending that larvicides should only be used:

- In general:
  - where breeding sites are few, fixed and findable.
- In sub-Saharan Africa:
  - 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;
  - in urban areas, because the breeding sites are more likely to be fixed, few and findable, and the intervention is more likely to be cost effective;

- 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.

As with IRS campaigns, larviciding requires careful planning, procurement of appropriate larvicides, application and protective equipment. Successful programme implementation can demand even higher skills than for IRS.

4.5 Technology landscape: space spraying

Description and policy on use

Space spraying or fogging is dispersion into the air of a diluted insecticide and is effective at killing vectors that come in contact with the insecticide while airborne. The technique is used for other vector-borne diseases such as dengue, but is recommended only in extreme circumstances for malaria control such as epidemics in urban areas or refugee camps.

4.6 Technology landscape: spatial repellents

Description and policy on use

A range of spatial repellents such as lotions, coils and passive emanators are sold on the consumer market. The products are mainly aimed at the nuisance insect market. Depending on the ingredients used in the products, they either repel insects or kill insects thereby reducing biting, which in turn may lead to decreased transmission of vector-borne diseases. There are no WHO-recommended spatial repellents, although the paradigm is under review by VCAG.

There is renewed interest in spatial repellents because they can have an effect on outdoor biting species or subspecies of mosquitoes. The core LLIN and IRS interventions are only effective against indoor feeding mosquitoes. It is believed that effective control of both indoor *and* outdoor biting insects will be needed in order to achieve elimination of malaria. Field trials of existing products and new concepts are under way to evaluate their effectiveness as malaria control tools.

4.7 R&D for vector control products: funding

R&D investment for vector control is essential in the strategy to control and eradicate malaria:

- to provide new tools to combat the threat of insecticide resistance;
- to improve the effectiveness and consumer acceptance of existing tools—e.g. IRS to long-lasting IRS (LLIRS);
- to provide new tools to address areas where current tools are ineffective or only partially effective (e.g. in reduction of outdoor transmission).

GMAP originally estimated that 3 novel active ingredient classes, 15 formulations and 3 new paradigms, such as larviciding, consumer products, etc., would be needed in the upcoming years to achieve malaria control and elimination [3]. Latest estimates by IVCC suggest a funding requirement of approximately US$ 600 million over the next 10 years is needed for a portfolio of similar size, with the development of new resistance-breaking active ingredients being the major driver of spending (Table 8). Beyond 2025, continued investment in R&D, albeit at reduced levels, will be needed to ensure new products are available if, or more likely when, resistance develops to the first wave currently in development.

Table 8: Estimated cost of R&D for vector control 2015–2025 and beyond

Timeframe	R&D stream	Total cost (US$ millions)
2015–2025	3 active ingredients	360
	10 formulations	80
	3 paradigms	100
	Other: new active ingredient screening, tools, information systems	60
	Total	**~600**
Subsequent 10-year periods	1 active ingredient	120
	5 formulations	40
	1 paradigm	40
	Other: new active ingredient screening, tools, information systems	100
	Total	**~300**

Source: IVCC, personal communication, September 2014.

Current spending on R&D for malaria vector control products, as reported to the G-Finder Survey conducted by the Policy Cures group, was US$ 31.2 million in 2012 [21]. In addition, chemical industry partners involved in IVCC projects are estimated to contribute approximately US$ 8–12 million per annum in materials and services.[12] The combined investment is equivalent to only around 7.5% of the overall R&D spending on malaria. Other key areas for malaria R&D spending in order of amount include basic research, drugs, vaccines and diagnostics.

The IVCC Product Development Partnership has the largest portfolio of potential new insecticides and formulations. The new insecticides in the IVCC portfolio are now entering stages of development that will require substantial increases in annual R&D spending, which is expected to come from the combination of donor and industry contributions.

There is relatively limited investment in innovation for vector control by the private sector. Interviews for this report consistently found that industry, including major players as well as small technology companies, regard the malaria vector control market as having an unfavourable structure and unattractive balance of risk and reward:

- approval timelines are complex, lengthy and costly;
- potential sales are relatively small (compared with crop protection insecticide targets);
- there are only a small number of donor purchasers, with no viable free market, making sales patterns uncertain and high risk;
- purchasers are highly price sensitive and find valuation of some innovations difficult (e.g. where innovations such an LLIN with synergists or long-life LLINs are available, there is reluctance to pay a price premium for the improvement due to difficulty in valuing the innovation);
- there is an easy “me-too” recommendation process based on simple chemical equivalence, which makes getting a return on investment for innovator companies very difficult and high risk.

The partners in the current IVCC projects are mostly large multinational corporations, whose involvement and contributions are underpinned by motivations associated with corporate social responsibility.

12 IVCC, personal communication, September 2014.

The reluctance to invest by private industry means there is a heavy reliance on donor funding to support R&D projects and rebalance the risk/reward profile. The concentration of funding by non-industry donors in malaria vector control R&D is high, with just five non-industry donors accounting for more than 80% of the total R&D funding in 2012 [21]. The top five non-industry donor funding organizations in decreasing order of funding supplied in 2012 are: the Bill & Melinda Gates Foundation (67%); the United States National Institutes of Health (NIH) (8%); the India Council of Medical research (3%), the Brazil Innovation Agency (3%); and the Wellcome Trust (2%).

4.8 R&D for vector control: pipeline

The R&D pipeline can currently be categorized into three main areas:

- existing paradigms—incremental improvements to existing tools;
- existing paradigms—new active ingredients;
- new paradigm tools.

Existing paradigms—incremental improvements to existing tools

This group contains innovations within existing paradigms that are relatively small improvements (such as reformulation) or additions to existing tools such as LLIN, IRS and larvicides. The more advanced projects in this class are being assessed by the WHOPES process (Table 9).

Table 9: Products under laboratory or field testing and evaluation by WHOPES

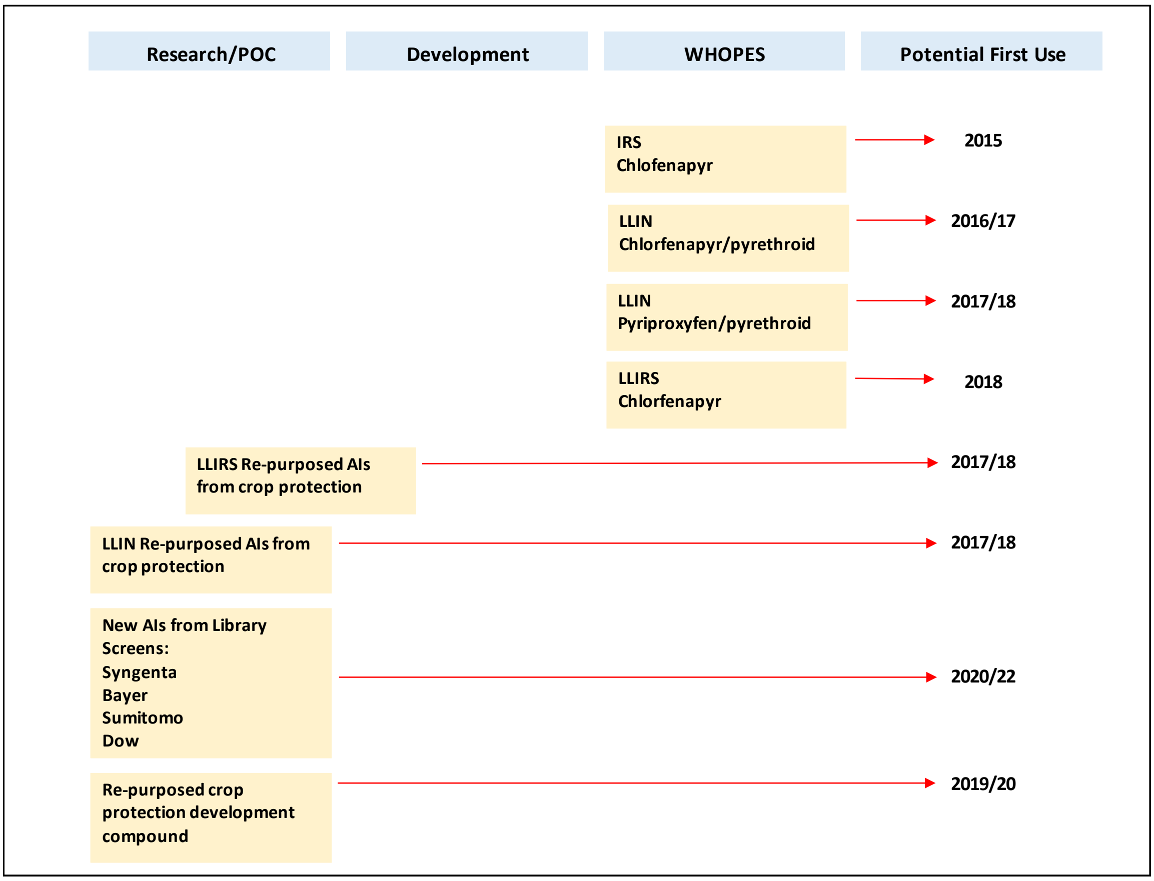
Application	Product
LLIN	Akanet LN DawaPlus 2.0 LN* LifeNet LN* Mapomel Safenet LN Miranet LN Olyset Plus LN** Olyset Duo LN Panda Net 2.0 LN PermaNet 3.0 LN** Veeralin LN Yahe LN
ITN treatment kits	ICON MAXX*
IRS	Alphacypermethrin SB
Larviciding	VectoMax GR

*WHOPES Phase I testing and evaluation.
**WHOPES Phase III testing and evaluation – contain synergist in addition to pyrethroid.
Source: WHOPES updated list of projects in evaluation of 28 March 2014.

Existing paradigms—new active ingredients

This group of projects aims to produce products that are primarily designed to address insecticide resistance. It contains active ingredients from insecticide classes not currently used in malaria vector control that are being evaluated and developed for malaria vector control use. Some of the active ingredients are already being used in crop protection or re-purposed for use in public health. Other active ingredients are completely new entities being developed specifically for public health use. A summary of the main projects is shown in Figure 6.

Figure 6: R&D pipeline new active principles*



* Other projects may be in evaluation or development within individual companies but have not yet been disclosed publically.
AI = active ingredient
POC = proof of concept
Sources: IVCC, September 2014. WHOPES updated list of projects in evaluation of 28 March 2014.

Most of the current activity in R&D of new active ingredients for use in the vector control sector is coordinated by IVCC, a Product Development Partnership, working with major agrochemical industry partners such as Bayer, BSAF, Dow, Sumitomo Chemical Co. and Syngenta.

The first of the crop protection-derived re-purposed active ingredients, a chlorfenapyr IRS developed by BASF, could be available for use within 12 months. In addition, LLIRS and LLIN presentations of chlorfenapyr are under evaluation.

Other active ingredients, resulting from re-purposing active ingredients used in crop protection or compounds identified from industry partner screens, are at earlier stages of evaluation and are still several years from potential recommendation and use. One private industry company is looking at a combination of three active ingredients in an LLIN to combat resistance.

In addition, the Foundation for the NIH has given four grants for target-based discovery of new active ingredients based on identification of novel sites of action (e.g. spider venom). These are very early stage exploratory research projects and, as such, are likely to suffer high attrition.

The activity and development of new active ingredients and the portfolio of projects are encouraging, but significant challenges must be overcome in development of new active ingredients before they can be used in the market:

- some active ingredients will fail to reach the market due to inadequate activity or adverse toxicological or environmental profiles;

- the process and time required for development and approval is uncertain:
    - new active ingredients may control vectors in a different way to existing products and will need new methods of assessment to be developed and agreed;
    - there is currently no internationally agreed pathway for regulatory approval of an insecticide developed specifically for public health.

New paradigm tools

In addition to developing new active principles, R&D efforts have been focusing on discovery and evaluation of new paradigms and approaches that have not been proven from a public health standpoint. Most are still in the evaluation and early development stages.

New paradigm projects include:

- spatial and personal repellents;
- attractants such as sugar baits combined with insecticides;
- patches impregnated with a non-pyrethroid insecticide that may be added to a bednet;
- mosquito traps;
- denetic modification of mosquitoes;
- biological modification of mosquitoes.

Some of these paradigms particularly target the control of malaria transmitted by outdoor biting. Addressing this aspect of transmission is likely to be very important. There is evidence from some previous eradication campaigns that a critical factor in the failure of eradication was incomplete suppression of outdoor feeding vector populations [22].

4.9 Evaluation and recommendation of new vector control products

Many of the countries that are subject to the highest levels of malaria have very limited capacity in vector control resources and in regulation of public health pesticides. In many cases, the in-country regulatory process lacks the capacity to perform a full evaluation of products; furthermore, the management of pesticides post-registration is also limited.

For these reasons, WHO along with a mandate from Member States, has established a system of evaluation, recommendation and monitoring of vector control tools.

VCAG and WHOPES are two of the most important systems that have been established. The functions of each group are summarized in Table 10.

Table 10: Summary of the jurisdictions of VCAG and WHOPES in vector control innovation

	VCAG	WHOPES
	Innovative vector control paradigms	**Innovative products from established vector control paradigms**
Scope	Looks at "first in line" prototypes when assessing paradigms claims. Does not evaluate individual product claims.	Evaluates individual product claims for commercially produced products.
Evaluation	Efficacy: requires entomological and epidemiological data. Safety: requires risk assessment. Other parameters, including target product profiles, user compliance/acceptability, economic feasibility, manufacturing sustainability and strategic/policy role.	Safety: requires risk assessment. Quality: WHO Specifications developed through Joint Meeting on Pesticide Specifications (JMPS). Efficacy: requires entomological data only.
Data	Reviews published and unpublished data submitted by the innovator.	Reviews data from WHOPES supervised laboratory and field trials according to WHO testing guidelines.
Outcome	Issues recommendations on the public health value of the paradigm and the associated first in line prototype to policy setting groups (Malaria Policy Advisory Committee [MPAC]/Neglected Tropical Diseases-Strategic and Technical Advisory Group [NTD-STAG]).	Issues recommendations on the efficacy, safety/risk and quality standards of public health pesticides for use by Member States for product registration and procurement.

Source: Second meeting of VCAG. Geneva: World Health Organization; February 2014.

These systems play an essential role in evaluating and recommending pesticide products as well as building in-country capacity for pesticide testing, evaluation and management. A recent survey showed that ~75% of WHO Member States rely, partly or solely, on WHOPES product recommendations for their pesticide registration decisions [23].

Given the urgent need for new vector control tools, particularly new active ingredients, it is essential that these systems work as efficiently and quickly as possible, while still providing a thorough evaluation.

VCAG is a relatively new system and still evolving. A recent paper [24] has set out a framework to enable efficient and rapid evaluation of new paradigms and new products for vector control.

The WHOPES recommendation process currently only addresses products for existing vector control interventions (IRS, ITNs/LLINs, space spray products and pesticide products for personal protection). When a new product is recommended by VCAG, WHOPES must establish relevant testing guidelines for safety and efficacy, make recommendations on use after its safety and efficacy assessment and develop specifications for its quality control and international trade.

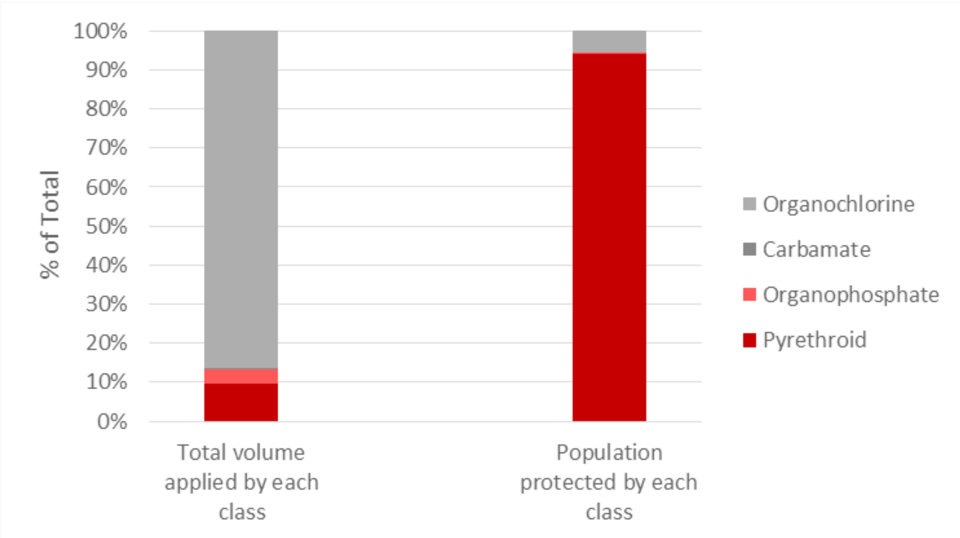
The ability of WHOPES to respond to a growing number and new types of products is critical to the success of accelerating the vector control R&D pipeline. This will require increasing the capacity of WHOPES in terms of both human and financial resources. Capacity must be increased not only within WHOPES, but also throughout the network of organizations that conduct assessments on its behalf [6]. Interviews conducted for this report found consistent viewpoints, expressed by many stakeholders in the vector control sector, that there are opportunities to reduce time to market by adapting the WHOPES system so that it continues to develop stringent standards and data requirements, but also accepts data generated for efficacy (providing it meets required standards) by industry. Many stakeholders on the supply side of innovative products believe it should be possible to make this change without losing the integrity or thoroughness of evaluation required to ensure products are effective and safe to use in the market. The handover of products from VCAG to WHOPES has not yet been tested, but interviews found that there is concern that there may be delays in this part of the evaluation process.

5 Market landscape

5.1 Market landscape: insecticides

Pyrethroids are by far the most widely used class of insecticides as measured by the number of people protected. Organochlorine insecticides are applied in higher volumes, but pyrethroids are used in very low dose rates of active ingredient in IRS and LLIN tools and so the resultant coverage and population protection by pyrethroids is much higher, as illustrated in Figure 7.

Figure 7: Share of insecticide class by volume applied and population protected



Source: Global insecticide use for vector-borne disease control, a 10-year assessment (2000–2009), fifth edition. Trioza Ltd analysis. Geneva: WHO; 2010.

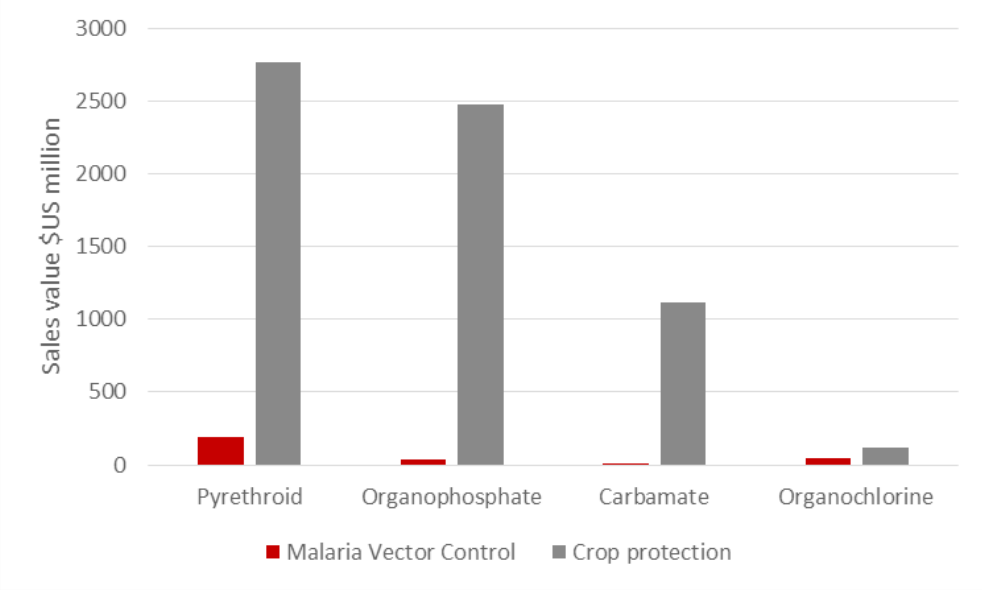
The latest WHO survey covers insecticide use by class until 2009. Since then, there have been some important changes in the insecticide class used:

- there has been a substantial increase in LLINs in the field, all using pyrethroid insecticides;
- there has been a shift away from use of pyrethroids towards organophosphates and carbamates in IRS due to concerns about insecticide resistance.

Due to the very high coverage provided by LLINs compared to IRS, the overall result would be a substantial increase in reliance on pyrethroids in terms of the number of people protected. Detailed analysis is not possible because current data on the insecticide class and volumes used in IRS are not available.

The main active ingredients used in vector control are also relatively widely used in crop protection, with the exception of organochlorines. In general, the volumes used in vector control are very low in comparison to the volumes used in crop protection as illustrated by the comparative market values (Figure 8).

Figure 8: Relative use of insecticide classes used in vector control and crop protection (2012)



Source: Phillips McDougall Global Agrochemical Service, Trioza Ltd analysis, 2012.

The insecticide active ingredients currently used in vector control (LLIN and IRS) no longer have patent protection on production and use of the active substance and may be manufactured by the originator company and other generic manufacturers.

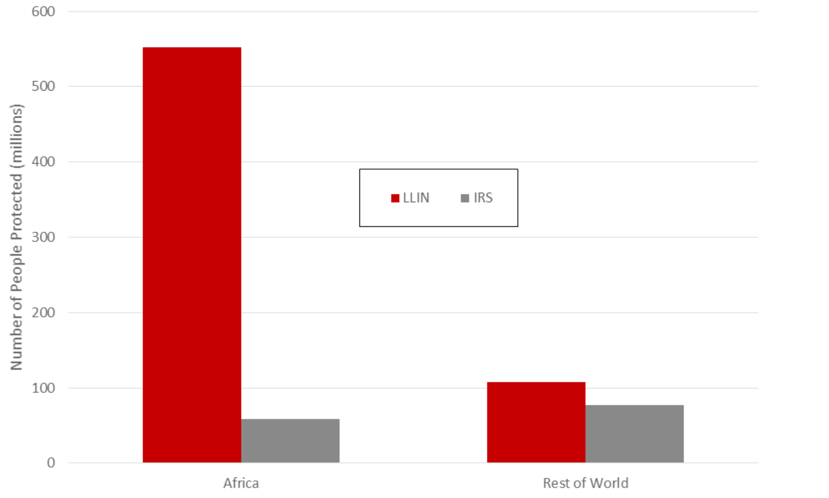
The combination of relatively low use volumes in vector control compared to crop protection, and multiple sources of manufacture means there are few market constraints on active ingredient supply for vector control.

It is possible the market may be constrained by downstream formulation or design patterns (e.g. a specific formulation providing long residual control; a specific design of an LLIN). In addition, some products (e.g. fenitrothion; malathion; propoxur) are not available in the market for vector control.

5.2 Market landscape: key interventions overview

Overall, in 2012, an estimated 785 million people were protected by insecticide-based malaria interventions. Around 650 million people are protected by LLINs, mostly in Africa, and around 135 million people are protected by IRS, spread more evenly across Africa and the rest of the world (Figure 9).

Figure 9: Number of people protected by major vector control interventions



Source: World malaria report 2013, Annex 4. Geneva: WHO; 2014.

In addition to the primary interventions of LLIN and IRS, supplementary protection in some countries will be provided by larval source management and space spraying. No coverage data are collected on use of these interventions, but they are believed to be far less in comparison with LLINs and IRS.

The cost model developed for GMAP [3] estimated that LLIN and IRS-based vector control would account for around 60% of total expenditure on malaria-related interventions (i.e. including case management and rapid diagnostic tests). Analysis of available data for this report estimates that around 45–55% of the US$ 2.5 billion from international disbursements and domestic sources in 2012 was allocated to vector control.

5.3 Market landscape: ITNs and LLINs

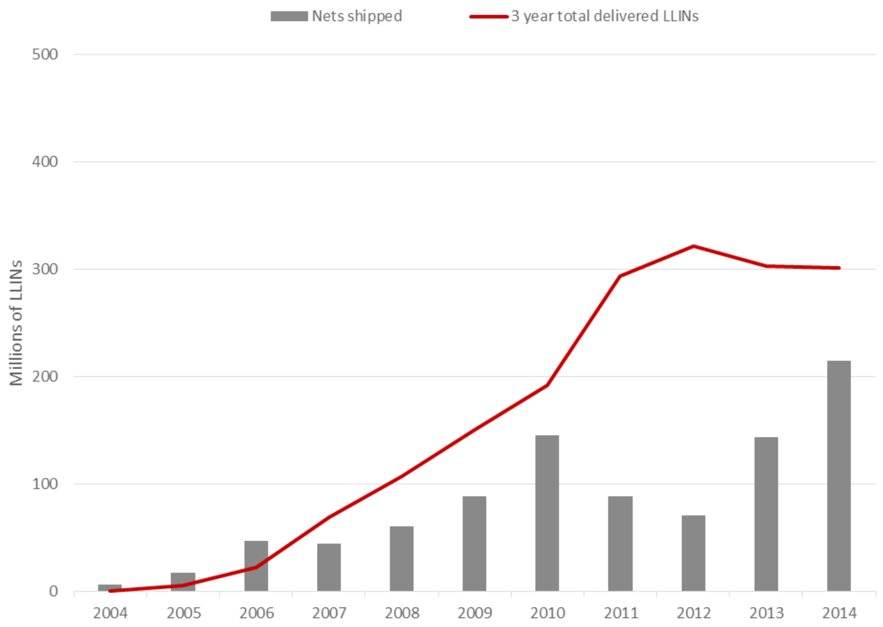
Coverage in Africa

There are approximately 800 million people at risk of malaria in Africa [1], which suggests the target for universal coverage, based on an average of 1.8 people per net, will require approximately 450 million nets to be in use each year. Based on the average net life of three years, approximately 150 million nets need to be delivered to end users every year in Africa to maintain universal coverage.

The numbers of nets delivered to the market, and theoretically still in use in the market, built up steadily until 2010. There was then a fall back of net deliveries in 2011 and 2012, mainly due to reduced purchases from the Global Fund. Delivery numbers have recovered substantially in 2013 to around 143 million (Figures 10 and 11) due to the resumption of Global Fund purchasing close to previous levels and increased purchases by PMI, but net numbers in the field are still well below the level needed for universal coverage. The latest RBM Gap Analysis[13] suggested that 223 million, 154 million and 201 million nets will be required in 2014, 2015 and 2016, respectively. Initial supply estimates suggest that approximately 215 million nets will be delivered in 2014 [25], leaving a gap of less than 10 million nets available for the following year.

13 RBM Harmonization Working Group. Global efforts to achieve and maintain LLIN coverage. Presentation at the Global Fund IRS Supplier Conference, Geneva, April 2014.

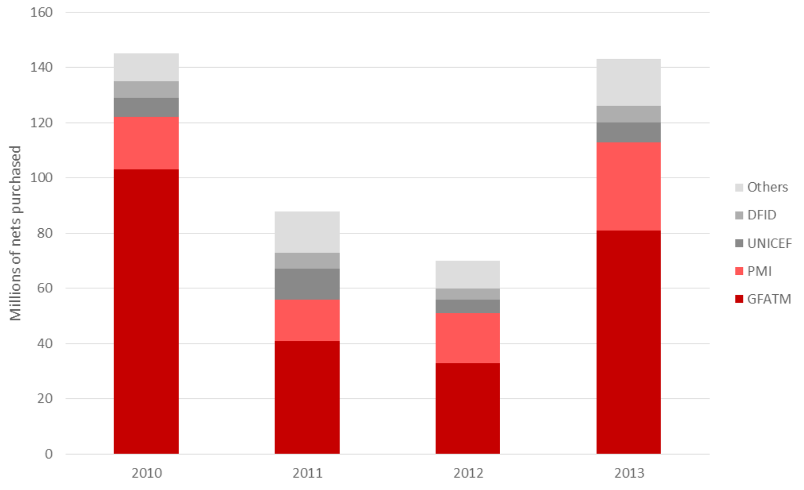
Figure 10: Number of LLINs shipped and cumulative useful nets* in the field in sub-Saharan Africa, 2004–2014



* Estimates of numbers of LLIN in use vary depending on the assumptions of net life and the lag between net shipment from the manufacturer to a country and final distribution to the end user. The methodology used in the chart for estimation of cumulative useful nets in use in the field is comparable with that used in the World Malaria Report 2013, in which WHO assumes a simple three-year life for each LLIN and a one-year delay from shipment to use in the field to calculate useful nets in the field. This methodology suggests around 300 million nets will be in use by the end of 2014; however, if it is assumed that nets are delivered very soon after shipment, then the number could be around 400 million nets in use.

Source: Data developed from Net Mapping collated by Milliner Global Associates. The delivery (i.e. shipment from manufacturers) of nets in the first three quarters of 2014 has been multiplied by 4/3 to provide an annual estimate for 2014.

Figure 11: Funding for LLIN in Africa by major donors 2010–2013



Sources: Data developed from Net Mapping collated by Milliner Global Associates, Global Fund PQR database, PMI and UNICEF reports.

Coverage in the rest of world

The requirement for nets in the rest of the world is less clear. Outside of Africa there are approximately 2.4 billion people at risk of malaria [1], which at a use rate of 1.8 people per net suggests a theoretical target of more than 1.3 billion nets that need to be in use each year to achieve universal coverage, with approximately 60% of the need coming from South-East Asia. Historically, there has been low coverage of donor or donor-provided nets because approximately 75% of the population in South-East Asia lives in low risk transmission areas [1]. At the end of 2013 there were around 80 million donor or publicly provided nets in use[14] outside of Africa. It is believed that some markets in South-East Asia have high levels of nets (combination of UTNs, ITNs and LLINs) in use purchased directly by users from the private market, but sources are largely anecdotal and no reliable estimates are available.

Funding

Currently, the LLIN market is very concentrated in terms of funding. The Global Fund and PMI account for more than 75% of purchases, with UNICEF, the World Bank and DFID the main purchasers of the remainder. Not all donors provide detailed breakdowns of prices, but based on total deliveries in 2013 of 165 million nets[3] at an indicative average price of approximately US$ 3.00 per unit [4], the total value of LLINs purchased by donors would be around US$ 500 million.

In order to maximize the procurement impact and access to LLINs, the Global Fund, UNICEF, DFID and the United States Agency for International Development (USAID) are collaborating through sharing and aligning forecasts and market analysis, as well as conducting joint tender briefings and developing a collaboration roadmap. The collaboration aims to provide enhanced visibility of long-term LLIN procurement, while operationally improving specification harmonization, price leverage and better coordination of planning and production schedules.

The Global Fund has made some important changes in its strategy and approach in terms of how it provides funding and how it makes purchases of commodities:

- The New Funding Model allocates funds to countries over a three-year period based on disease burden and income. Countries then develop plans and proposals for allocating the funds between AIDS, tuberculosis and malaria and interventions for each disease. The first proposals for countries have been considered by the Global Fund; and there do not appear to major changes to the proportion of funds countries decide to allocate to LLIN (or other interventions such as IRS).[15]
- The Purchasing for Impact Programme (P4i) aims to deliver better value for money in purchasing but also tries to help suppliers, particularly smaller companies, through setting up two-year contracts, rather than tender by tender purchases, to improve visibility, production and capacity planning.[16] Tender evaluations are made using a combination of commercial factors, such as price and delivery performance, and non-commercial factors, such as advantages through innovation or additional services. The weighting given to non-commercial factors is approximately 16%.

These changes are still recent and it is not yet possible to evaluate their impact on the market. Initial feedback from industry suppliers is supportive of the concept of a more collaborative approach and longer term contracts but some have raised concerns about the process being less transparent than its predecessor, with little feedback when their application fails.

Suppliers that provide innovative LLINs are extremely concerned that donors in general still put too much emphasis on purchasing at the lowest possible unit price to the detriment of innovation and cite the lack of purchase of LLINs higher priced products containing synergists (to provide improved control where pyrethroid resistance is present) or nets made from polypropylene (to provide longer net life) as examples. One major supplier with substantial historical investment in vector control R&D is considering withdrawing a product from the market due to lack of purchases. Donors generally acknowledge they are cautious about

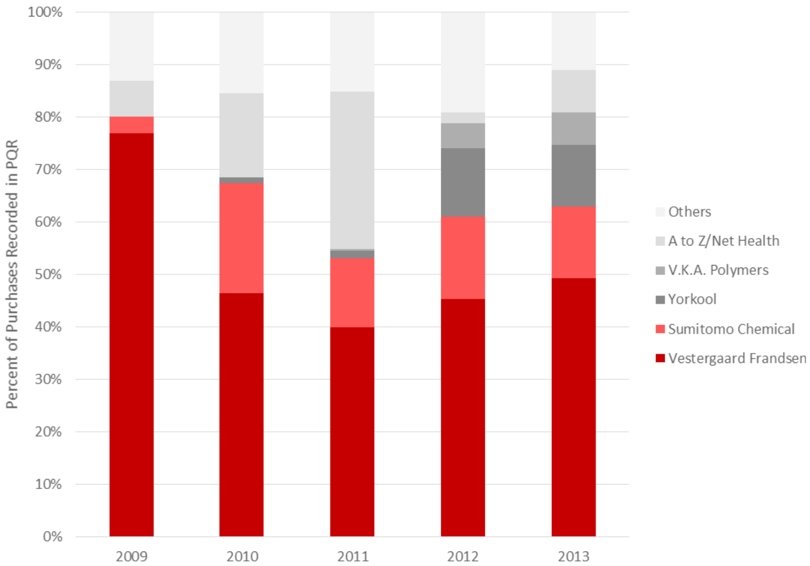
14 Milliner Global Associates, Net Mapping Project, Trioza Ltd estimates, personal communication, July 2014.
15 Jan Kolaczinski, Global Fund, personal communication, 6 November 2014.
16 Global Fund. LLIN update. Procurement and Supply Chain Management (PSM) Working Group (WG) meeting, Geneva, June 2014.

purchasing new innovations, citing the reasons that agreed standards beyond the minimum WHOPES requirements and data proving value for money of novel products are not always available or consistent enough to enable full assessment.

Supply

The number of suppliers has grown substantially in recent years. There are now 10 companies with WHOPES-recommended nets, with a further five nets and four suppliers currently progressing through the WHOPES system. Data from the Global Fund Price and Quality Reporting (PQR) databases show that from 2009 to 2013 two suppliers, Vestergaard Frandsen and Sumitomo Chemical Co., accounted for approximately 65% of total nets supplied, with the remainder split between other suppliers (Figure 12).

Figure 12: Split of LLIN by supplier as recorded in the Global Fund PQR, 2009–2013*



*2013 data are not yet complete.

Source: Global Fund PQR transaction database.

Data on the split of supply between manufacturers in the 2013/2014 season are not yet publicly available, but initial disclosures suggest that purchases are more evenly spread across the supplier base.[17]

Current estimates of supply capacity for WHOPES-recommended LLIN range from 240 to 300 million units per year for standard net sizes.[18] Purchases of non-standard sizes require more production time per unit and can reduce overall production capacity. This level of capacity appears to be more than sufficient to cover the 150 million LLINs for Africa and existing levels of LLIN purchases for the rest of the world, but this needs to be viewed with caution:

- The capacity is likely to be sufficient, providing the offtake of nets is spread evenly throughout the year; but if offtake is concentrated over part of a year, then capacity may be insufficient in these circumstances.
- It is not clear what the levels of sales outside of donor programmes are. These sales would compete for production time.
- If demand outside Africa grew substantially, then capacity may be insufficient.
- Some suppliers may have outsourced production to production sites that have now obtained their own LLIN recommendation—capacity estimates could be double counted.

17 Global Fund. LLIN update. Procurement and Supply Chain Management (PSM) Working Group (WG) meeting, Geneva, June 2014.
18 A major LLIN supplier estimated capacity at 240 million units. UNICEF estimated capacity at 300 million standard size units in the Long Lasting Insecticidal Nets Supply Update, May 2014.

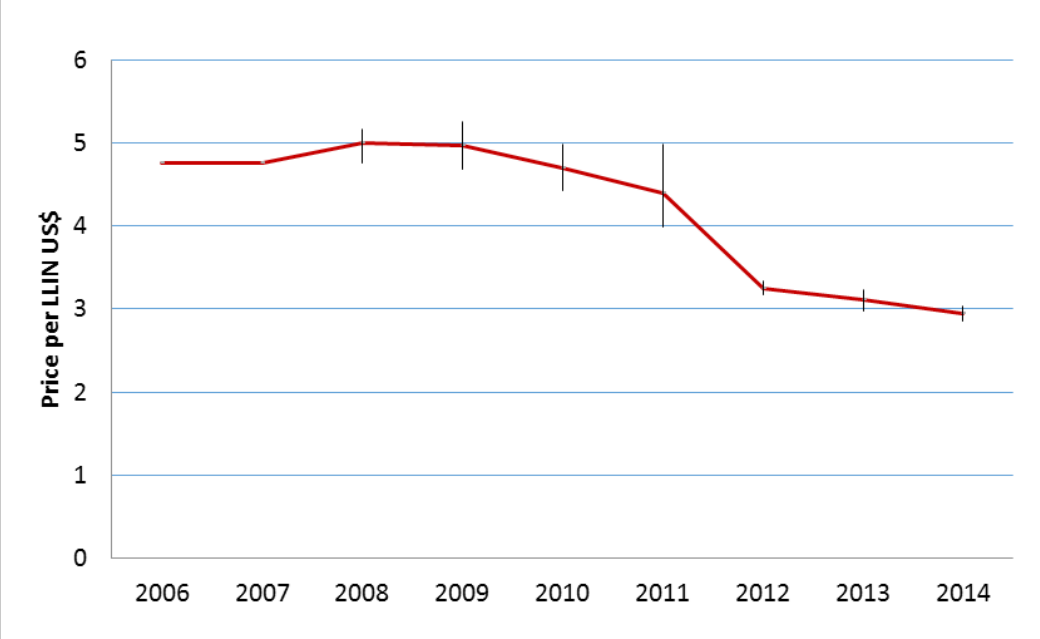
This important component requires further investigation and analysis.

Cost of a delivered LLIN

The main driver of the final cost of an LLIN delivered to an end user, normally representing 50–55% of the overall costs of a delivered net, is the purchase price of the LLIN itself.

UNICEF, one of the leading procurers of LLINs, publishes regular information on its purchase prices for LLINs. The average price for nets purchased by UNICEF fell by over 40% during the period between 2008 and 2014 and now stands at US$ 2.95/net (Figure 13) [4]. A Global Fund analysis presented in 2013 indicated their prices have dropped 45% since the third quarter (Q3) of 2009 from US$ 5.56 to US$ 2.90 per net.[19]

Figure 13: UNICEF—evolution of prices of 190x180x150 cm LLIN, 2006–2014



Source: Price transparency report. New York: UNICEF; August 2014.

The decreasing price of LLINs can be attributed to variety of factors such as:

- The increase in volume of purchases of nets, enabling savings through a manufacturing scale effect.
- Reduced prices achieved through the pooled tender process.
- Increased market competition as the number of WHOPES-recommended suppliers has increased from 1 in 2002 to 10 in 2014. New, generic suppliers also can benefit from "me too" equivalence test procedures that allow them to reach the market with substantially lower costs. Technical advances may have also played a part.

The rate of price reductions has slowed over the last two years. The likely cause of the slowing trend in price reduction is a combination of production scale reaching the level of maximum cost efficiency and supplier profits falling to minimum acceptable levels. Some manufacturers claim that their production costs are above the purchase price. One major LLIN manufacturer supplying a Global Fund tender, on an open book basis, claims to have made less than 5% profit and has actually shown losses on some shipments due to raw material cost increases. Industry sources suggest that the man-made fibre is the major raw material component of costs, accounting for around 50–65% of the total raw material costs and is

19 C Game and M T Jallow. The Global Fund: "Where are we today and our new approach to supplier management". Presentation at the Global Fund IRS Supplier Conference, Geneva, May 2013.

subject to substantial price volatility related to the price of oil derivatives.[20] Other major costs components include the insecticide (5–10%) and direct manufacturing costs such as labour and energy (20%), R&D amortization, overhead, transport and taxes/duties. At current levels of profitability, there is a risk of withdrawal from the market of some producers, leading to a reduction in available capacity.

Beyond the net itself there are significant additional costs of delivery, training, overhead, personnel and distribution. The RBM Gap Analysis tool assumes that, based on a purchase price of US$ 3.30 per net, the final cost of delivered net to an end user is around US$ 5.80/unit [26]. Using the RBM delivered cost of US$ 5.80/net with a three-year net life, and an average of 1.8 people per net, the cost to protect a person for one year with an LLIN is approximately US$ 1.00 per person.

It has been suggested that mass campaigns have the lowest median cost per net delivered compared with other delivery channels [27]. The true, fully loaded cost to deliver a bednet will vary substantially by country or area and can be driven by social costs—e.g. behaviour modification and communication costs—as well as the necessary logistical requirements for delivery.

Distribution

National malaria control programmes (NMCPs) in the African Region reported using mass campaigns as the main LLIN distribution channel during 2012, accounting for 89% of nets distributed, followed by antenatal care clinics (7%), immunization clinics (3%) and other channels (2%) [1]. Approximately 87% of LLINs outside Africa were reported to have been distributed through mass campaigns, 6% through immunization clinics, 1% through antenatal care clinics and 6% through other channels [1]. Most nets are provided to the end user free of charge: out of the 99 countries that reported ongoing transmission, 88 provided nets free of charge and 16 reported some distribution at subsidized prices.

WHO recommends that mass distribution is complemented by continuous or "routine" distribution through multiple channels, in particular antenatal and immunization services [28]:

- Mass distribution campaigns are a cost-effective way to rapidly achieve high and equitable coverage, and in almost all settings repeated campaigns will be needed. As coverage gaps start to appear almost immediately post-campaign through net deterioration, loss of nets and population growth, complimentary continuous distribution channels should be in place.
- The interval between mass campaigns should normally be no more than three years unless there is reliable observational evidence that a longer interval is appropriate (e.g. routine distribution through antenatal care and expanded programme on immunization (EPI) channels is maintaining high coverage; nets are lasting longer).
- Where possible, there should be a gradual shift in the methods used to distribute LLINs away from campaigns and towards continuous distribution systems providing the primary means of sustaining coverage.

Analysis and experience in the use of continuous distribution systems is growing year by year:

- A study in the United Republic of Tanzania in 2011 concluded that a voucher-based system distributed through schools, child welfare clinics and antenatal care clinics could provide a good level of coverage to maintain net numbers in the field [29].
- In 2013, the NMCP in the eastern region of Ghana piloted a mixed model of LLIN distribution combining "push" distribution through child welfare clinics and antenatal care clinics at primary schools with "pull" distribution using subsidies delivered through E-coupons to encourage consumer net purchases. The model appears to have been highly effective in maintaining coverage [30].

Further investigation is needed to identify how and where continuous distribution systems should be developed beyond existing levels.

20 Trioza Ltd estimate based on interviews with LLIN suppliers and analysis of raw material costs.

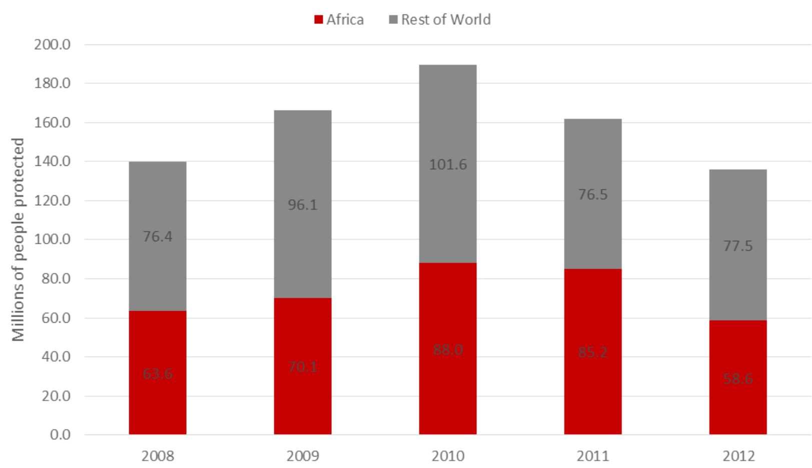
The level of sales of LLIN through the private sector in Africa appears to be very limited. Discussions with some of the major suppliers of LLINs suggest that current private sales volumes in Africa are approximately 1–2% of the volumes supplied through donor campaigns. Suppliers see little opportunity for this to change in the near term due to the huge distortion to the market caused by free of charge donor distributed nets. One supplier in the United Republic of Tanzania sells significant quantities (around 15–20% of the annual demand to provide universal coverage for LLINs) of UTNs through private retailers. A UTN retails at around US$ 2.50/net versus an LLIN at US$5.00/net. This suggests there may be opportunities, in some markets, to create some level of user purchased market for LLINs through a price subsidy scheme.

5.4 Market landscape: IRS

Market trends

WHO estimates that approximately 136 million people were protected by IRS in 2012. Since 2010, there has been an overall 30% reduction in the number of people protected (Figure 14).

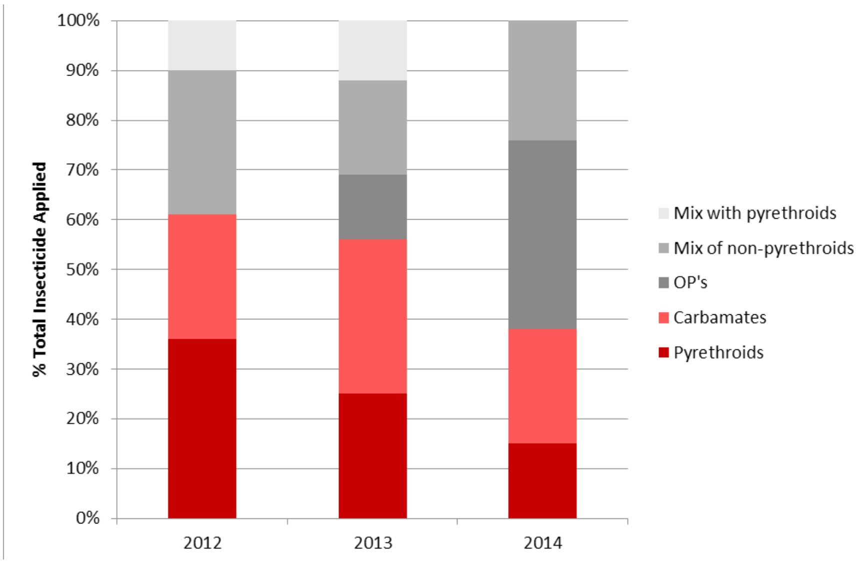
Figure 14: Number of people protected by IRS 2008–2012 [1]



Detailed data on IRS insecticide use in all countries are not available to enable a definitive analysis of the cause of the reduction in use. However, it appears the evolving response to insecticide resistance is at least one of the major factors responsible. Until 2010, pyrethroids were the dominant class of insecticide used in IRS because they provide excellent persistence and low cost. The increasing problem of resistance to pyrethroids is causing IRS programmes (in particular PMI-funded programmes that are very active in promoting data-driven insecticide selection based on susceptibility data and IRM) to use organophosphate and carbamate insecticides (Figure 15), which are significantly more expensive. For example, in the PMI Africa Indoor Residual Spraying (AIRS) Project, typical average costs of the insecticide components to spray 100 metres^2 are US$ 1.72 for pyrethroids, compared to US$ 5.82 for carbamates and US$ 7.91 for organophosphates [31]. Given relatively fixed budget levels allocated to IRS, this appears to be resulting in a reduction in the number of structures sprayed and people protected. A number of countries are likely to stop using IRS completely in 2014 due to pyrethroid resistance and affordability of alternatives.[21]

21 IVCC, personal communication, September 2014.

Figure 15: Insecticide use by class in PMI IRS programmes, 2012–2014



Source: Kristen George. PMI Indoor Residual Spraying Programme. Presentation at the Global Fund IRS Supplier Conference, Geneva, April 2014.

Currently, the only way to apply a non-pyrethroid insecticide in resistance management is by use of IRS. If the cost of insecticide continues to be a major constraint on use, then the ability to make progress in the fight against insecticide resistance will be put at severe risk.

Funding

There are only limited data available on funding of IRS. The largest financers of IRS are country governments and PMI and the Global Fund are the two major international donors involved in IRS. PMI estimates their IRS programmes protected 21.8 million people (equivalent to 5.5 million dwellings) in 2013.[22] The Global Fund estimates having spent approximately US$ 7.5 million on IRS in 2013 and the planned PMI spending for 2014 is approximately US$ 90 million.

Supply

There is very limited information regarding suppliers of IRS insecticides. Many of the active ingredients recommended for use in IRS by WHOPES are produced by both the originator and generic manufacturers. The more basic formulations of products, such as wettable powders (WPs), suspension concentrates (SCs) and emulsifiable concentrates (ECs), can be made by most competent pesticide manufacturers. The major issue is whether the products can be consistently manufactured to meet the WHO specifications for each recommended formulation. Failure of products to meet specifications has been highlighted as an issue by some donors, particularly the Global Fund. Experience from the crop protection sector suggests that this may be a consequence of the cost-driven purchasing processes; the low prices mean that tenders are being won by generic suppliers with lower quality production and quality control systems or that receive low priority in production schedules of larger originator companies. In addition, IRS products are often purchased through many small tenders, which makes supply planning difficult for manufacturers.

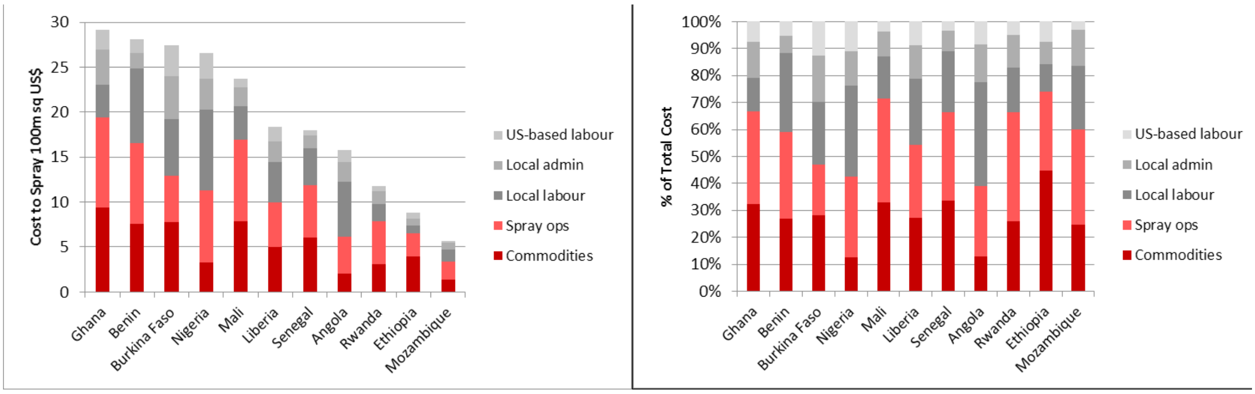
Several new IRS products that use novel slow-release formulations that extend product persistence after application (LLIRS) have been introduced or are in the R&D pipeline. These formulations are more complex to produce in order to meet required performance in the field and may reduce the number of suppliers able to produce and supply the LLIRS. In addition, some formulations may be protected by patents or proprietary know-how that may restrict the supply to the patent holder or technology originator.

22 Kristen George. PMI Indoor Residual Spraying Programme. Presentation at the Global Fund IRS Supplier Conference, Geneva, April 2014.

Cost to implement/deliver IRS

Unlike LLINs, where the cost of the net is the dominant component of the overall delivered cost, the cost components that make up IRS are more balanced between the cost of insecticides and operational costs. PMI provides a detailed breakdown of costs in 11 of the markets in which it operates. The analysis shows significant variation in the level of costs between different countries (Figure 16).

Figure 16: IRS programme costs and cost breakdown in PMI AIRS Project in square metres, 2012



Source: Africa Indoor Residual Spraying (AIRS) Project. IRS country programmes: comparative cost analysis of 11 August 2011–31 December 2012. Washington DC: PMI, USAID.

The main measure used to compare costs is the cost to spray 100 metres² (typical size of a house for a small family). There are significant variations in the costs to spray 100 metres² depending on the country, and PMI analysis suggests that the main reasons for this are:

- Choice of insecticide class (costs of different product classes are given above) accounts for around 20% in the total variation in costs between countries.
- Scale and country context. Large-scale programmes benefit from economies of scale, but only if spraying operations are concentrated; if operations are highly dispersed, then the cost of transport, warehousing and spray application can be significantly increased. Wage levels also differ between countries.

Spray commodities account for 24% of total costs on average. The insecticide accounts for more than 80% of total commodity costs, with the sprayer and personal protection equipment making up most of the remaining 20%.

The PMI study found that 9 out of the 11 countries surveyed used only *one* application of IRS and the average cost to protect a person for one year was approximately US$ 5.00, with a range of approximately US$ 2.00–12.00. (Note: Some of the products used, e.g. carbamates, may not have sufficient persistence to provide full protection throughout the transmission season).

5.5 Market landscape: other tools

There is a substantial market for consumer insecticide products such as aerosols, coils, mats and vaporizers. According to a Euromonitor study in 2013, the global value of the consumer product market for mosquito control at the retail level was US$ 5.6 billion in 2013, of which Africa and the Middle East accounted for under 10%. The insecticide component of this will be very small. A large majority of these products are targeted at nuisance pests in the home. Their impact on malaria transmission is not known.

6 Market shortcomings and their reasons

6.1 Situation analysis—key issues

Pressure on funding

Donor purchases of LLINs in 2013 and 2014 have stabilized the overall level of nets in the market, but this level is still short of the target for universal coverage, even in the most severely affected region of Africa.

The limited availability of funds has resulted in a high emphasis being placed on value for money and unit price of vector control commodities. While this has been successful in reducing unit cost, particularly of LLINs, prices have been driven down to levels of marginal economic viability for suppliers and could result in some higher cost suppliers withdrawing from or reducing supply to the market.

The pressure on donor budgets also makes purchases of any higher priced innovative commodities difficult, unless there is full and consistent evidence demonstrating value for money. The limited purchases of some recent innovations have led several major suppliers to conclude that donors are not willing to pay for innovation and are discouraging a few major suppliers from investing in R&D to develop innovative products.

Growing threat of resistance

There is a widespread distribution and growing intensity of insecticide resistance to all of the currently available insecticide classes used in the primary IRS and LLIN tools. Pyrethroid resistance is one of the fastest growing in intensity due to the widespread use in IRS and LLINs. There is a growing risk that the effectiveness of current interventions is being eroded and may result in increased levels of malaria transmission.

It is essential for all malaria-affected markets to understand the extent and impact of resistance and to put in place strategies to limit the damage to malaria control. However, progress in IRM has been limited, and appears to be hampered by a lack of capacity and funding that may be related to the complexity of valuing the cost–benefit of IRM spending.

There are limited intervention tools available to manage resistance, and those that are available, such as IRS programmes using organophosphates or carbamates, are more expensive on a per person basis than LLINs or pyrethroid IRS programmes. However, there is some evidence that where high levels of pyrethroid resistance are present, switching to an IRS programme with a non-pyrethroid can provide improved levels of control of malaria transmission and may provide better cost–effectiveness if considered on the basis of the reduction in malaria transmission per US$ 1000 spent.

Progress is being made to bring to the market new classes of active ingredient that are effective against current forms of insecticide resistance. The vector control market is not seen as an attractive commercial target by industry, so it is essential that donor co-funding is available to finance R&D, particularly early high-risk phases. Further measures to accelerate acceptance and use of new products in the market may also be needed, particularly as new products are likely to be more expensive than existing intervention tools.

The first of the new products to combat resistance—chlorfenapyr—is close to market; other products could be available within three to five years. It is essential that routes to evaluate field efficacy, human and environmental safety and cost–effectiveness are clearly defined and as efficient as possible so that new products can reach the market as quickly as possible.

Distribution

Currently, the most widely used intervention, LLINs, relies heavily on periodic, often thrice-yearly or more, mass campaigns. While effective in attaining initial levels of coverage, this approach is something of a "blunt instrument"; it cannot respond to the gaps that occur due to loss of nets through damage or to nets that still have a useful life when a new campaign starts. The role of routine distribution systems to replace nets needs to be developed to ensure coverage is maintained so that funds are used as efficiently as possible.

6.2 Summary of shortcomings

A series of specific shortcomings that relate to these key issues are described in Table 11.

Table 11: Summary of vector control shortcomings

<table>
<tr><th>Category</th><th>Shortcoming</th><th>Reason</th></tr>
<tr><td rowspan="3">Availability</td><td>Lack of new products and paradigms, particularly to address resistance and durability concerns.</td><td>■ Manufacturers reluctant to invest in R&D due to:
◆ uncertainty around whether or not there will be a willingness to pay for the innovations, as the market is very price sensitive;
◆ metrics to differentiate innovation in net-based products (e.g. longer efficacy; increased durability; insecticide resistance mitigation) are not in place beyond the WHOPES minimum quality standards;
◆ their perception that R&D costs will be difficult to recoup because "me too" equivalent products will undercut reference product prices before R&D investment is paid back and rewarded;
◆ evidence of the health impact and effectiveness of new paradigms will be difficult, expensive and time consuming to generate.</td></tr>
<tr><td>Innovative products face difficulties reaching the market in a timely fashion.</td><td>■ Improved tools to address resistance, durability and outdoor transmission challenges will require at least two to three years in the WHOPES process to reach the market.
■ WHOPES may not have sufficient capacity to operate to a faster timescale while maintaining quality.
■ Interface between VCAG and WHOPES not yet tested.
■ Some delays are caused by manufacturers providing products that are of unsuitable quality for testing.
■ Unclear metrics to differentiate products and measure innovations.</td></tr>
<tr><td>No products with proven ability to control disease transmission from outdoor biting.</td><td>■ Not viewed as priority to date.
■ Work now being funded by the Bill & Melinda Gates Foundation.</td></tr>
</table>

Affordability	Higher cost of products for resistance limits uptake.	■ Resistance-breaking tools are more expensive than base pyrethroid treatments. Budgets are limited, resulting in reduced coverage or continued use of pyrethroids. ■ Insufficient large-scale use data to demonstrate value for money. ■ Implementation metrics focus on coverage rather than disease averted per US$ 1000 spent.
Quality	Reduction in effectiveness of existing products by insecticide resistance.	■ Limited implementation of GPIRM strategy in the field, due to: ◆ limited choice of products available for use to combat resistance; ◆ lack of on-the-ground expertise and capacity in countries; ◆ the cost–benefit of combating insecticide resistance is not widely understood, resulting in inadequate funding being allocated for implementation.
	Uncertain linkages between LLIN durability, field life and value for money.	■ Durability and effectiveness of any product varies significantly by region, making it difficult to predict durability. ■ Existing strength tests are poor predictors of field performance. ■ Donors are unwilling to purchase “longer lasting” nets at higher prices until performance is fully validated.
Acceptability	Limited uptake of IRS in contrast to LLIN.	■ IRS programmes are complex and costly to implement. ■ Metrics focus on coverage versus disease averted per US$ 1000 spent.
Delivery	Risk that some established LLIN suppliers may exit the market.	■ Innovator companies believe that the focus on lowest cost procurement by concentrated donor buyer groups has driven down prices from suppliers to levels that do not provide returns adequate enough to reward the cost of capital of the R&D-based industry. Current prices paid for nets are only sufficient to sustain generic producers with low overhead and no innovation to reward.
	Difficulty shifting to a consumer-driven market.	■ LLIN market distorted by donor-supplied free nets in mass campaigns.
	Potential significant gaps in coverage in some areas outside of Africa.	■ Current donors have not focused scale-up efforts on populations that have the potential to purchase protection products on their own (i.e. population segments in South-East Asia).

7 Potential interventions

As discussed above, there are multiple, interrelated market shortcomings and challenges facing the vector control community. This section is not specific to the UNITAID mandate and business model, but rather represents a range of market-based interventions that could be undertaken by different global health actors and stakeholders.

The potential interventions that have been identified are described in Table 12.

Table 12: Description of potential interventions

Category	Shortcoming	Potential intervention
Availability	Lack of new products and paradigms, particularly to address resistance and durability concerns.	■ Co-fund R&D, particularly in earlier high-risk stages. ■ Provide advanced market commitments sufficient to reward industry investment in R&D for innovations targeted at specified critical areas such as resistance management insecticides suitable for use in LLIN. ■ Consider providing innovators a minimum period of exclusive sales, as done in agricultural markets, in order to allow for return on R&D investment.
	Innovative products face difficulties reaching the market in a timely fashion.	■ Consider changes to WHOPES that may reduce time needed for evaluation and recommendation, including acceptance of industry data, provided they meet certain defined standards. ■ Accept prequalification of the safety and environmental data package of new active ingredients by major regulatory agencies (e.g. Environmental Protection Agency; European Union). ■ Assess if provision of extra funding to increase capacity would improve the speed of evaluation and recommendation. ■ Appoint independent project "guides" to facilitate project progress through WHOPES. ■ Set up online system for VCAG and WHOPES project review consultation, with quarterly meetings of small core groups to make decisions. ■ Consider setting up a fast track country registration for a product with WHOPES recommendation.
Affordability	Higher cost of products for resistance limits uptake.	■ Fund purchase of initial sales to enable: ◆ generation of large-scale use data that demonstrate cost–effectiveness under field conditions to enable purchase by major donors; ◆ building up production and batch scale to improve affordability.

Quality	Degradation of existing products by insecticide resistance.	■ Provide more resources for IRM to support: ◆ development of new products to combat insecticide resistance; ◆ identification where new tools (such as synergists) can be used; ◆ implementation of the Framework for National Insecticide Resistance Plans; ◆ dedicated expert support where needed; ◆ development of cost–benefit models and communications to ensure funding is allocated to IRM.
	Uncertain linkages between LLIN durability and field life value for money.	■ Develop new tests and metrics that more accurately predict field performance and life. ■ Fund studies and/or initial sales of "higher durability" nets to enable generation of large-scale use data that demonstrate cost–effectiveness under field conditions to enable purchase by major donors. ■ Donors purchase nets that provide best lifetime value for money, even if this is at a higher unit price. ■ Educate users on best practice for net use and care.
Acceptability	Limited uptake of IRS in contrast to LLIN.	■ Co-fund IRS in high transmission areas where LLIN intervention is not effective or where net use levels are poor (e.g. areas where pyrethroid resistance is at high levels of intensity and there is evidence of poor disease control).
Delivery	Risk that some established LLIN suppliers may exit market.	■ Recognition that quality and innovation generates extra costs that require higher prices to reward. Open book accounting can be used to validate profit margin.
	Difficulty shifting to a consumer-driven market.	■ Conduct an analysis to identify where it may be appropriate to encourage the development and sustenance of retail sector by use of voucher schemes to deliver nets in routine distribution programmes. ■ Conduct an analysis to identify where it may be appropriate to fund a pilot programme with subsidized retail sales of LLIN in a market with current retail sales of UTN.
	Potential significant gaps in coverage in some areas outside of Africa.	■ Fund study to understand extent of coverage, including consumer purchased products.

8 Appendix 1: References and acknowledgements

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9 Appendix 2: Profiles of major stakeholders

There are several key stakeholders in the vector control commodities space, including manufacturers, R&D funders and drivers as well as donors and multilateral organizations. Profiles of the major R&D funders and drivers, donors and multilateral organizations are found below.

9.1 R&D stakeholders

Bill & Melinda Gates Foundation

The primary funder for malaria vector control R&D is the Bill & Melinda Gates Foundation, which has identified malaria as one of its top funding priorities. During 2008–2012, it invested US$ 131 million in malaria vector control R&D, with plans to invest another US$ 81 million during 2013–2015. It also works with global partners to support efforts to expedite malaria research beyond vector control, expand access to life-saving drugs and prevention methods and advocate for greater action in the development of vaccines, prevention strategies, drugs and public awareness. It is one of the two dominant funders of malaria research overall, along with the United States NIH.

As far as vector control is concerned, it has an important partnership with IVCC, for which it is the main funder, directing over half of its vector control funds. However, it is also involved with various other projects in the vector control domain, including those looking into WHOPES, net durability and resistance.

IVCC

IVCC, established in 2005, is a Product Development Partnership aiming to overcome the barriers to innovation in the development of new insecticides for public health vector control and to develop information systems and tools that will enable new and existing pesticides to be used more effectively. They also work with disease endemic country stakeholders and industry to establish target product profiles for new paradigms in vector control. IVCC is the primary recipient of funding from the Bill & Melinda Gates Foundation for vector control; between 2007 and 2010, IVCC received approximately 55% of the foundation's funding.[23]

R&D-based companies

Several of the major agrochemical companies have long-established vector control programmes, notably BASF, Bayer, Sumitomo Chemical Co. and Syngenta. All of these companies are working with IVCC, with a combined annual R&D spending of approximately US$ 10 million.[24] They also view vector control as very much a niche market, and without the partnership with IVCC the overall level of the R&D effort they would be likely to devote to vector control would almost certainly be far lower.

23 Global funding of innovation for neglected diseases. G-FINDER; 2013 (http://g-finder.policycures.org/).

24 Personal communication with representatives from BASF, Bayer, Sumitomo Chemical Co. and Syngenta.

9.2 Donors

Global FundThe Global Fund was established in 2002 to dramatically increase resources to fight the devastating diseases of AIDS, tuberculosis and malaria. It is a public–private partnership working as an international financing institution dedicated to attracting funds and directing them to areas of greatest need. Since its inception and until December 2013, the Global Fund has received over 90% of its funds from governments.

The Global Fund brings together at the country level a wide diversity of implementing government bodies, international development partners (including UN agencies and donors), national civil society organizations (including local media, professional associations and faith-based institutions), the private sector and communities living with or affected by these diseases.

Regarding malaria vector control, the Global Fund has been the key driver for the major scale-up of ITN delivery. By December 2013, it had funded the distribution of more than 300 million nets (ITNs and LLINs). It also has supported IRS for more than 40 million houses.[25]

PMI (USAID)

PMI was established in 2005 as a five-year, US$ 1.2 billion expansion of United States government resources to reduce the burden of malaria and help relieve poverty on the African continent. It is an interagency initiative led by USAID and implemented together with the United States Centers for Disease Control and Prevention of the United States Department of Health and Human Services.

The goal of PMI is to reduce malaria-related deaths by 50% in 19 countries in Africa that have a high burden of malaria by expanding coverage of four highly effective malaria prevention and treatment measures to the most vulnerable populations. In 2008, the programme received an increase of up to US$ 5 billion in PMI funding for five more years, aiming to halve the burden of malaria in 70% of at-risk populations in sub-Saharan Africa.

PMI works closely with a wide variety of organizations, including host country governments, other United States government agencies, international organizations, other bilateral, multilateral and private donors, NGOs, faith-based organizations and the private sector.

Vector control supported initiatives include ITNs and IRS. In its 2013 financial year, PMI sprayed over 5.5 million houses with insecticide, protecting 21.8 million people, and procured over 40 million LLINs.[26] The number of houses sprayed declined from the previous year due to the increased costs of insecticides used. Alternatively, the number of LLINs increased as PMI stepped in to compensate for the temporary decline in purchases by the Global Fund.

UNICEF

UNICEF plays a key role in many global, regional and country malaria partnerships. It is a founding partner and key board member of RBM. UNICEF is also strengthening partnerships in malaria with the World Bank, PMI, the Global Fund, Malaria No More and UNITAID. In recognition of malaria's role as one of the biggest killers of children in Africa, prevention and control interventions form an integral component of a minimum package of the UNICEF high-impact maternal and child survival interventions.

UNICEF is one of the largest purchasers of LLINs, buying over 238 million nets between 2002 and 2014. Together with its partners, UNICEF distributes LLINs through routine health services and campaign approaches. It also works with ministries of health and NGOs.

25 Global Fund. Progress reports: the Global Fund; 2013 (www.theglobalfund.org/en/publications/progressreports/ and PQR transaction database).
26 PMI. Seventh annual report to Congress. Washington DC: PMI; 2013.

9.3 Multilateral organizations

WHO

WHO is the directing and coordinating authority for health within the UN system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends.

WHO hosts the Global Malaria Programme, which provides the community with policy guidance and annually publishes the World Malaria Report, a document that consolidates the status of the fight against malaria.

WHO also hosts WHOPES, which, since its establishment in 1960, has been serving as a reference for setting norms and standards for public health pesticides and their life-cycle management for the entire malaria community for all vector-borne diseases. In 2012, WHO established VCAG with the remit of evaluating new paradigms and categories for vector control.

RBM

RBM was launched in 1998 by WHO, UNICEF, the United Nations Development Programme and the World Bank in an effort to provide a coordinated global response to the disease and to halve the world's malaria burden by 2010. It is comprised of more than 500 partners, including malaria endemic countries, their bilateral and multilateral development partners, the private sector, NGOs and community-based organizations, foundations and research and academic institutions.

The RBM overall strategy aims to reduce malaria morbidity and mortality by reaching universal coverage and strengthening health systems. GMAP defines two stages of malaria control: (i) scaling-up for impact (SUFI) of preventive and therapeutic interventions; and (ii) sustaining control over time. In 2008, world leaders and the global malaria community endorsed GMAP, which provides a global framework for action around which partners can coordinate their efforts.

RBM has been holding a Vector Control Working Group (VCWG) since 2003, with the purpose of facilitating the alignment of partners on strategy and "best practices" to rapidly scale up malaria vector control interventions, particularly ITNs and IRS, in order to meet targets for malaria control. The VCWG has several work streams according to the challenges the vector control community is currently facing:[27]

- Insecticide resistance
- Outdoor malaria transmission
- Continuous LLIN distribution systems
- Durability of LLINs in the field
- Capacity-building for IRS
- Larval source management
- Optimizing evidence for vector control interventions
- Entomological monitoring and integrated vector management (IVM)
- Housing and malaria.

27 Vector Control Working Group (VCWG). Roll Back Malaria; 2013 (www.rollbackmalaria.org/mechanisms/vcwg.html).