Final publishable summary report MCD Project

Executive Summary

The EU-FP7 funded Mosquito Contamination Device (MCD) project was executed between 1 December 2012 and 30 November 2015. The overall aim of the project was to develop low-cost devices that can lure, infect and/or kill malaria mosquitoes. At the start of the project, twelve concepts for MCDs were contemplated, of which six were subsequently prioritised based on advice from the project's External Advisory Board. During the second half of the project and based on R&D outcomes from the first eighteen months, the focus was further narrowed to three prototype MCDs: The Eave tube, the Smart Patch, and the Outdoor Host-seeking Device (OHD).

The Eave tube exploits the natural host-seeking behaviour of African malaria mosquitoes, which preferentially enter houses through the open space between the roof and walls (the so-called eave). When these eaves are closed and eave tubes are installed every 1-1.5 m the natural airflow and ventilation inside the house is maintained. Host seeking mosquitoes respond to odours from house occupants that emanate from the tubes. When they enter the tubes they encounter insecticide-treated electrostatic netting that has resistance-breaking potential. This MCD was advanced to such an extent that it was implemented in the field in close to 1900 houses in southern Tanzania. The Smart Patch also exploits the natural host-seeking behaviour of malaria mosquitoes. Mosquitoes tend to orient towards odour-laden convection currents of bednet occupants and therefore end up on the ceiling of the net above the head and torso where they make contact with the netting. Therefore, nets can receive a small 'patch' or 'strip' on the ceiling as part of a two-pronged strategy: untreated nets receive a patch of LLIN material in areas where pyrethroid resistance is absent, or LLIN nets receive a non-pyrethroid treated patch in areas where pyrethroid resistance is intense. The third MCD is the Outdoor Host-seeking Device, for which various models that make use of attractive (human odour) blends were tested and developed, as a means to curb the problems associated with increased outdoor biting in areas where indoor interventions (IRS/LLINs) have selected for (partial) outdoor biting.

A novel electrostatic coating onto which insecticidal particles can be bound through polarity was developed. Results against strains of malaria mosquitoes from across Africa show that application of electrostatically adhered particles boosts the efficacy of WHO-recommended insecticides, even against (pyrethroid-)resistant mosquitoes. Eave tube development successfully progressed from idea to production-ready and field-validated product prototypes. Through the MCD project RTD and demonstration activities, proof-of-concept and field validation was achieved in Kenya and Tanzania. Eave tube coverage reached 79% in Mngeta in southern Tanzania, where now close to 10.000 inhabitants receive additional protection against malaria mosquitoes. Community acceptance was excellent and it was shown that eave tubes provide a low-cost, effective and resistance-breaking intervention that can be integrated in malaria vector control programmes. This novel technology will be further advanced via additional field demonstrations (funded by UKAid/HDIF), a Phase 3 RCT in Ivory Coast (funded by BMGF), mass-production developments and commercialisation activities by consortium members. Smart Patches show promise as a cost-effective tool to augment bednet efficacy; a small netting strip on top, comprising only 3% of the total surface area, can improve mosquitocidal impacts with 50% and boost personal protection, even against resistant mosquitoes. Smart Patches can be deployed on untreated nets or on LLIN nets as a cost-efficient means to apply novel resistance-breaking chemistries and augment impacts of LLINs. Research on Outdoor Host-seeking Device prototypes showed that stand-alone devices without the need for electricity can successfully attract and kill malaria vectors by deploying passive-release odour lure dispensers augmented with CO_2 mimicking chemicals and electrostatic netting with insecticides. These would have most potential in push-pull frameworks, which are currently being developed through several R&D collaborations.

Summary description of project context and objectives

Project context

Malaria remains the world's most significant infectious parasitic disease, with an estimated 438.000 deaths (range 236 – 635 thousand) and 214 million cases (range 149-303 million) in 2015. Between 2000 and 2015, malaria incidence rates (new malaria cases) fell by 37% globally, and by 42% in Africa. During this same period, malaria mortality rates fell by 60% globally and by 66% in the African Region[1]. These significant advances in control were mainly the result of improved vector control (LLINs and IRS) and use of good medicines (ACTs). Nevertheless, malaria still poses a public health crisis in many countries with a huge socio-economic impact in many low-income developing countries. There is still no commercially available vaccine and parasite resistance against medication is a growing problem, particularly in SE Asia. The only other option is to target the vector of disease: the malaria mosquito. Current methods focus primarily on killing adult mosquitoes with chemical insecticides through Indoor Residual Spraying (IRS) and long-lasting insecticide-treated bednets (LLINs). These tools provide personal protection against mosquito bites via physical protection, repellency and lethality, but can only be deployed indoors and thus lose their efficacy when malaria vectors alter their behaviour to biting and resting outdoors. Today, insecticide resistance is regarded as the single most significant threat to the sustained control of mosquito-borne diseases, including malaria. Over the last decade physical and behavioural resistance has been reported against all four classes of WHO-recommended insecticides across Africa and other continents. This is a major and growing threat to the effectiveness and sustainability of contemporary malaria vector control measures as well as the public health gains accrued over the last fifteen years. It is therefore imperative, particularly in view of the fact that malaria elimination and eradication is foreseen within the next 25 years, to develop new vector control tools and means to incorporate these in integrated vector management strategies.

Aims and objectives

Given these developments, the Mosquito Contamination Device ('MCD') Project had as its primary aim to develop novel vector control devices that can be deployed in the tropics to effectively lure, infect and contaminate malaria mosquitoes. The goal was to create new tools with resistance-breaking potential that can be used in integrated vector management (IVM) programmes to complement or augment current measures and at the same time counter the challenge of insecticide resistance. The MCD project focused on low-tech and low-cost devices that attract mosquitoes via passively released synthetic odour lures and contaminate them with lethal doses of insecticidal compounds (biological or chemical) upon contact. The project consortium combined expertises in the fields of mosquito behaviour and ecology, insect bait technology, coating and application methods, materials sciences, design and prototyping, and field research/operations. The original idea was to combine slow-release attractants with novel combinations of (biological) insecticides, namely fungus and juvenile hormone analogues, in portable outdoor point-source devices. Based on promising results and recommendations from the project's External Advisory Board, non-portable and non-outdoor devices as well as new applications of WHO-recommended public health insecticides were also included.

The main scientific and technological objectives were to:

- Select insecticidal agents (bioactives) and combinations thereof that can effectively kill insecticide-resistant *Anopheles* mosquitoes even after short and transient contact;
- Develop long-lasting bioactive applications for use in MCDs that can persist under tropical climate conditions;
- Prototype and optimise low-cost, low-tech and user-friendly MCD designs that are attractive to anophelines;

[1] World Health Organization. World Malaria Report 2015.

- Augment the attractiveness of MCDs by adding synthetic mosquito lures and develop long-lasting passive odour release techniques;
- Evaluate and optimise the efficacy of MCD prototypes under controlled and ambient climate conditions in semi-field environments (large outdoor cages/screen houses);
- Evaluate the attractiveness and impacts of MCDs under open field conditions in Tanzania and beyond;
- Test MCDs in a push-pull or integrated frameworks;
- Demonstrate and/or model potential malaria vector control impacts of promising MCDs.

MCD project activities were divided into 6 Work Packages with the following objectives:

Main Objectives	Specific Objectives
1. Management To achieve effective project collaboration and coordination	1.1 Project management and steering 1.2 Monitoring and reporting scientific and technical progress 1.3 Contractual and financial management follow-up
2. Infectants & Contaminants To develop effective and long-lasting applications for mosquito-killing bioactives	2.1 Develop infective and long-lasting bioactive formulations 2.2 Create formulations with optimal transfer and mosquito contamination 2.3 Achieve effective and long-lasting combination applications
3. Attractive device To develop a low-tech, low-cost device that effectively lures malaria mosquitoes via passively released odours and other attractive stimuli	3.1 Collate and evaluate scientific knowledge on mosquito attractants and traps 3.2 Design a point-source device that is attractive to anophelines 3.3 Develop effective, long-lasting passive-release odour lures 3.4 Develop a MCD that lures mosquitoes close enough to enable efficient fungus and JHA pick-up
4. Integration of MCD components To effectively integrate all separate MCD components and evaluate and optimise its long-lasting efficacy in realistic (semi-field) settings	4.1 Evaluate long-term efficacy bioactive formulation prototypes in semi-field 4.2 Evaluate placement and attraction of point source device prototypes in semi-field 4.3 Evaluate & optimise long-term MCD efficacy in semi-field 4.4 Evaluate integrated use of MCDs and ITNs
5. MCD Demonstration To present and demonstrate our best prototype MCD at other places in Africa	5.1 Execute MCD demonstrations in existing semi-field setups at research institutes in other countries 5.2 Demonstrate MCD efficacy outside Tanzania in limited open field trials
6. Dissemination To distribute and propagate the project's results globally and enable successful future MCD implementation	6.1 Developing a project web site 6.2 Promoting knowledge transfer & capacity building 6.3 Patenting foreground IP 6.4 Commencing collaborations with industrial partners

At the start of the project, an elaborate dissemination strategy was designed, including dissemination and exploitation activities aimed to address appropriate knowledge transfer, as well as intellectual property management and dissemination of project outcomes to key stakeholders and the general public. To ensure optimal communication and knowledge sharing, we used an online database platform and organised 2-3 day project meetings on a biannual basis to evaluate results and discuss overall strategies with the Consortium members. Project management was organised by the Work Package leaders, whom held regular Skype meetings, and was augmented by strategic advice from our External Advisory Board consisting of knowledgeable scientists and stakeholders.

Main Scientific & Technological results and foregrounds

MCD prototype selection

At the launch of the MCD project 12 concepts for MCDs were contemplated, of which 6 were subsequently prioritised based on advice from the External Advisory Board. During the second half of the project, the focus remained on 3 prototype MCDs: The Eave tube, the Smart Patch, and the Outdoor Host-seeking Device (OHD). These devices are all robust and low-cost designs that combine an attractive lure and a biocidal agent that can be integrated and provide effective mosquito control.

- The **Eave tube** exploits the natural host-seeking behaviour of African malaria vectors, which enter houses through the eaves, which is the open space between the roof and walls of houses. By closing the eave and installing eave tubes every 1-1.5 m, the natural airflow is maintained, and mosquitoes respond to host odours emanating from the tube. When they enter the tube they are blocked from entering and can be contaminated and killed when contacting the insecticide-treated netting.
- The **Smart Patch** also exploits the natural host-seeking behaviour of malaria mosquitoes around bednets; making contact with the ceiling of the net where body odours and convective heat concentrate. Small dark netting 'patches' or 'strips' on the ceiling can be used to effectively target anopheline mosquitoes with novel chemistries away from direct human contact.
- The **Outdoor Host-seeking Device**, consisting of small portable point-source designs that make use of attractant (human odour) blends and can be deployed outdoors as well as indoors.

Electrostatic netting

A novel exposure technique based on an electrostatic coating principle that binds multiple insecticidal compounds in powder form was developed. This electrostatic coating enabled deployment of several types of insecticidal particles on netting material and significantly improved dose transfer to mosquitoes – even to those that make only short and transient contact with the netting. We visualised this by showing that high quantities of fluorescent dust particles are transferred to the mosquito body and become visible under UV light even after only 5 seconds of contact with the netting (Figure. 1).

Fig. 1. *Anopheles mosquito contaminated with fluorescent dust particles after short contact with electrostatic netting*

The originally selected actives (fungus spores and pyriproxyfen) significantly reduced survival of mosquitoes after short contact with the netting and pyriproxyfen was actively picked up and transferred (disseminated) to breeding sites under laboratory conditions. Because the majority of the MCD prototypes focused on targeting host-seeking anophelines, it was decided to select and test several fast-acting and more persistent WHO-recommended insecticides. Deltamethrin and bendiocarb powder were considered most suitable for use in MCD prototypes.

The electrostatic netting against pyrethroid-resistant malaria vectors was evaluated in collaboration with the Liverpool School of Tropical Medicine (UK) and the Vector Control Reference Unit of the NICD in Johannesburg (South Africa). Mosquitoes were exposed in bioassays to electrostatic netting dusted with deltamethrin in amounts similar to or lower than the insecticide dose used in standard coated bednets (Permanet 2.0). In total, mosquitocidal impacts for 13 different mosquito strains of all important mosquito genera (*Aedes, Culex* and *Anopheles*) that originate from 11 different countries were compared. Four susceptible and six pyrethroid-resistant mosquito strains of the major malaria vectors *Anopheles arabiensis*, *An. funestus* and *An. gambiae* s.s. that originate from nine countries in Africa were tested (Figure 2). Results showed that the adulticidal impact of deltamethrin applied on electrostatic netting was significantly higher for all resistant *Anopheles* strains compared to impacts induced by standard bednet material. Figure 2 shows that eave tube netting effectively curbed pyrethroid resistance in the resistant strains. Even 15-fold lower insecticide doses were effective in killing resistant mosquitoes and confirmed that the electrostatic netting has an optimal bioavailability causing high dose transfer of insecticide to the insect.

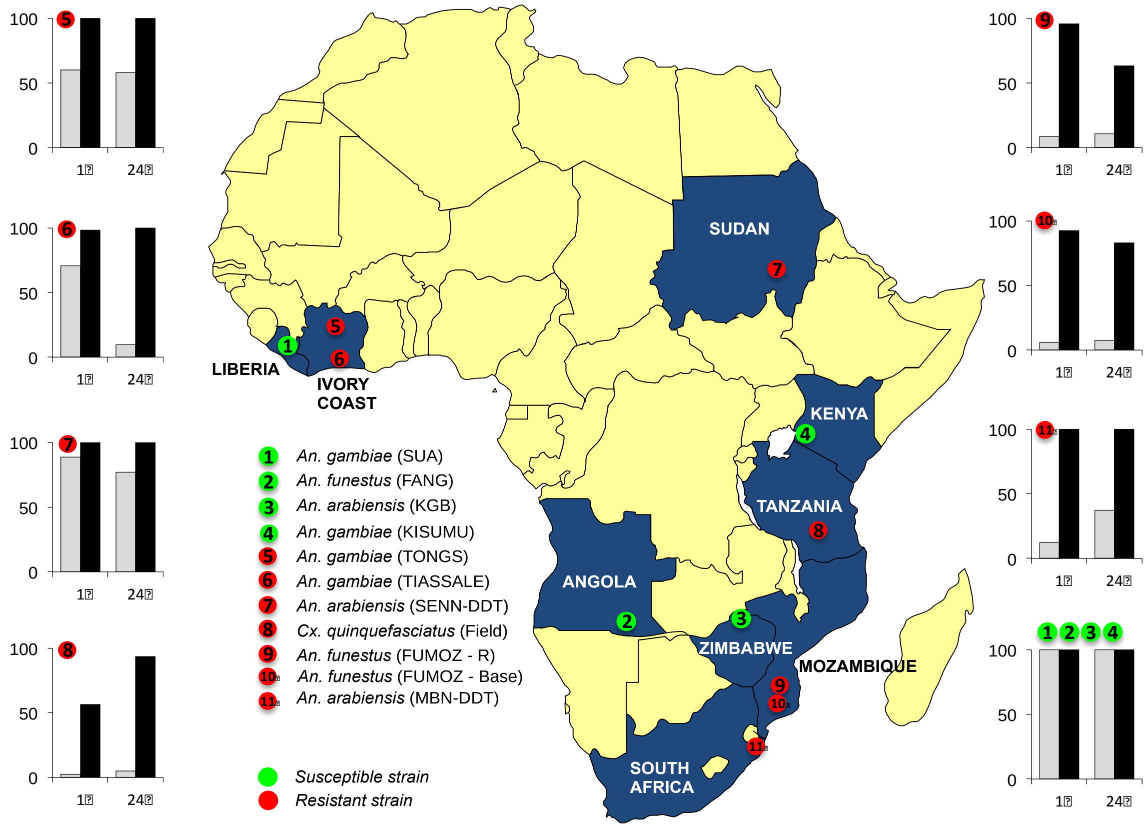

Fig. 2. *Origins and resistance status of tested mosquito strains (red = resistant, green = susceptible). The bar graphs show survival impact after 3-min exposure (1 = 1 hr knockdown; 24 = 24 hrs mortality) to a standard Permanet bednet (55 mg deltamethrin/m^2; grey bars) or electrostatic netting with deltamethrin (37 mg/m^2; black bars).*

The resistance-breaking effect was most likely due to the increase in the effective contamination dose, which exceeded the quantity that can be tolerated by resistant strains. This work was published in the high impact journal *Proceedings of the National Academy of Sciences, USA* (*Andriessen et al., PNAS 2015)* and provided proof that electrostatic netting increases insecticide transfer to such an extent that even resistant mosquitoes can be killed effectively. MCDs that deploy this electrostatic netting (such as Eave tubes) can thus boost the efficacy of WHO-recommended insecticides, which can help stimulate their uptake as a novel resistance-breaking vector control tool.

Long-lasting insecticidal residues on electrostatic netting

Several methods for powder application were explored, using as low as possible insecticide doses. A standardised and quality-controlled method to homogenously apply insecticidal powders on electrostatic netting was developed, which can be used in large-scale manufacturing and (re)treatment processes. Results showed that shaking provided the lowest quantities of insecticide dust in highly homogenous layers (Figure 3) with excellent particle retention after treatment: no powder was released, even at high wind speeds. These application doses were still highly effective to kill mosquitoes and persist over time. We customised a low-tech and low-cost insecticide quantification method that helped to assess and optimise product persistence by enabling direct measurements of the quantity of actives on netting.

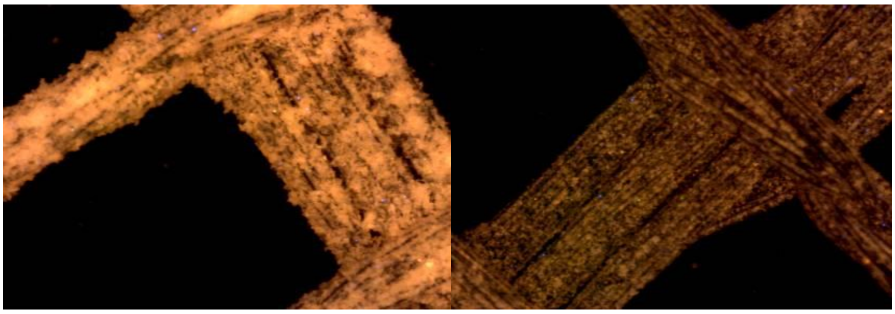

Fig. 3. *Fully saturated netting binds 14 grams of fluorescent dust/m^2 (left) and shaken netting binds only 6 grams/m^2 (right). Magnification 250x.*

A range of field persistence studies in Tanzania showed that spores of the fungus *Beauveria bassiana* remained virulent under tropical conditions for periods of up to 2 months. This could be a feasible treatment period for easy-to-replace Eave tube inserts or be suitable in areas where the transmission season is relatively short (like in the Sahel), but we also decided to focus on more stable chemistries and tested deltamethrin and bendiocarb insecticide dusts. Persistence results showed that bendiocarb loses its mosquitocidal efficacy under field conditions within 4-6 weeks when applied inside Eave tubes, whereas deltamethrin has potential to last for at least 4 months. Even though field-collected samples showed dust and smoke particles adhering on the treated netting, these did not interfere with the transfer and efficacy of the deltamethrin particles. Field studies indicated that pyrethroid-treated electrostatic netting has a high persistence and can provide a long-lasting application that is comparable with standard IRS treatments (that last for 3-6 months).

Odour lures & attractants

Several chemical and physical stimuli (i.e. odours, colours, patterns, humidity, and heat) that may be of use in MCD designs were identified. These were evaluated over short range inside mosquito cages or in room tests with free-flying mosquitoes. Heat and human skin odours were the most important stimuli for inducing mosquito landing responses, which is needed to achieve MCD contact and mosquito contamination. Several artificial odour blends, like the "Ifakara" and "Mbita" blend, were tested. Nylon strips, impregnated with natural foot odour or artificial blends, were attractive to host-seeking females when tested inside OHD prototypes. We did not utilise odour lures in Smart patches or Eave tubes, since mosquito attraction to these devices was shown to be high even in the absence of supplemental odour lures, because they benefit from existing odours emitted by bednet/house occupants Commercially available powder formulations of attractants made from natural sources, including meat extract powder and bacterial growth agar, were also tested. These may be deployed on electrostatic netting. Nevertheless, to date the research on lure and kill devices baited with electrostatic netting loaded with meat extract powder showed that these were as effective as devices baited with the gold standard attractant; a worn sock. Novel low-tech and low-cost passive release technologies for attractants were developed. Different materials were evaluated to determine their suitability as slow-release dispensers for mosquito attractants: nylon fabric, impregnated plastic granules and permeable membrane pouches. Nylon fabric was shown to be suitable for water-based odour lure applications and released small amounts for at least 4 months. A technology was developed to cheaply incorporate different attractive substances (both lipophilic and hydrophilic) into polymer granules at low temperatures. The polymer itself is hydrophobic, which prevents (rain) water from washing the actives out of the granules. It is possible to charge granules up to their own weight with attractants. Dyes and chemical indicators can also be incorporated into

Fig. 4. *Permeable membrane pouch containing slow-release polymer granules loaded with three different attractive components.*

the granules to visualise the mix ratio and to show if the attractant is still present. Granules can be mixed in any ratio, which enables the use of a wide range of compounds in defined proportions. These can be used to fill air-permeable sachets or other dispensers (Figure 4). Sterilicin membrane pouches were evaluated and showed that these can release water-based odours lures passively for several months to attract malaria mosquitoes. These membrane dispensers were also effective for deploying the polymer granules and improved their persistence. Slow-release polymer granules inside membrane dispensers were shown to disperse mosquito attractants for more than 9 months under field conditions in Tanzania. This odour release technology showed to be useful for Outdoor MCD field deployment as it augmented their attraction and improved their mosquitocidal efficacy. Field tests showed that this new granule-based system was already competitive in efficacy and persistence with commercially available mosquito lure dispensing systems. Results to date demonstrate that the MCD odour release technology provides a low-tech, low-cost and effective means to deploy odour lures in passive, stand-alone devices and augment their attraction to malaria mosquitoes.

MCD designs

We developed the 'Eave tube' concept whereby simple holes are drilled at eave level into which 6-inch PVC tubes with netting inserts (Figure 5) can be placed. Like eaves, these tubes allow human odour-laden air to pass through them and thus attract mosquitoes into them. Once inside the tube, the mosquitoes encounter a physical barrier; a coated netting from which they pick up insecticidal particles that kill them when they make contact with it. Eave tubes are simple tools that can be fitted in all types of houses, work passively and use only small amounts of insecticides away from direct human contact. Eave tube semi-field tests showed that tubes installed at 180 cm above ground level (20 cm under the roof) were significantly more attractive than tubes placed lower to the ground. Horizontally placed 6 inch PVC tubes of 20 cm long were most effective and provided a feasible installation option. We advanced the Eave tube design towards durable and simple-to-install insert components that can be mass-produced cost-effectively via injection moulding (Figure 5). The conical shaped inserts can be manufactured from strong and flexible polypropylene and can be easily stacked for transportation. The spokes, protruding node and stabilizing wings provide additional support and easy placement inside tubes. Eave tube insert casings are fitted with electrostatic netting with customised overmoulding processes that embed the netting into the casing. These techniques enable cost-efficient mass production of durable inserts. We also made progress in developing mechanisms for applying fixed doses of insecticide on insert stacks via automated triaxial shaking machinery, which shows promise for use in large-scale automated production systems. Since the netting inserts are robust and durable, they can be re-used. Recycling of inserts is achievable through simple washing and re-treatment processes. Scale economies will dictate eventual product pricing, as several factors will determine the depreciation and overall production costs.

Fig. 5. *Final design of the Eave tube: consisting of gauze inserts that can fit into locally sourced PVC tubes of different thickness.*

We are already taking steps to move towards the use of re-cycled polyethylene bednet materials or other forms of biodegradable plastics as the ingredient for the injection moulded insert casings. These steps will allow us to eventually deliver a high quality, sustainable and low cost product for malaria vector control.

The Smart Patch was designed as a small insecticide-treated patch of netting added to the top of a bednet, to provide a simple, cheap, and easy-implementable technology. This was based on the known behaviour of host-seeking malaria mosquitoes inside the house; they search primarily along the top of the net on a restricted area above the head and chest, trying to gain access to the host. Multiple Smart Patch types and materials were tested, including different sizes (Figure 6), colours and shapes. The best results were obtained with black polyester netting strips on top of the bednet ceiling. Proof-of-concept studies showed that a small Smart Patch made from standard impregnated LLIN material, added on top of a non-treated net can create a cheap alternative to fully treated LLINs; achieving 50% of the impact for only 1/3rd of the cost of an LLIN. Validations in South Africa showed high mortality impact of bendiocarb-treated Smart Patch strips on top of an LLIN; these significantly boosted mortality rates of highly insecticide-resistant malaria mosquito strains. Sewing a Patch strip into the top of the netting was effective and considered as the most feasible fixation option and the best choice for future mass-scale Smart Patch production.

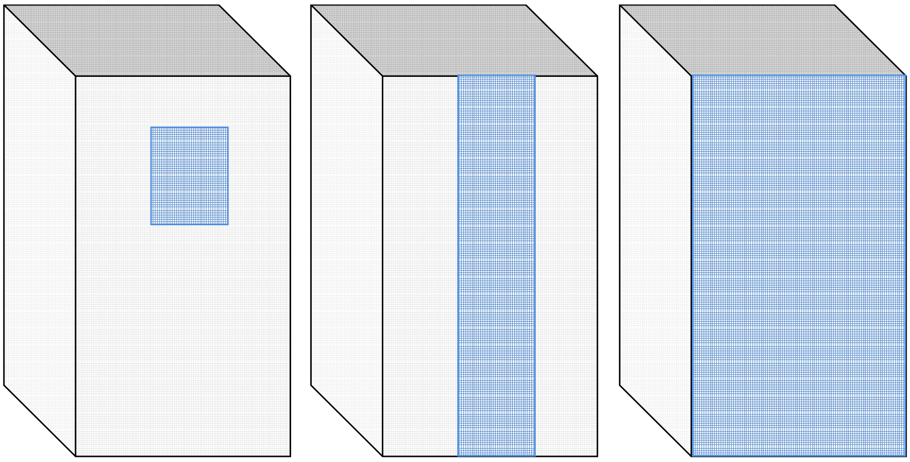

Fig. 6. *Smart Patch prototypes; (a) A 30 cm x 60 cm piece placed on top of a bednet, (b) a 30 cm wide strip running from the head to the foot end, (c) a patch covering the full top of a bednet.*

The Outdoor Host-seeking Device (OHD) was designed as a small, portable device that can be operated in-and outdoors near houses/cattle sheds and lure mosquitoes by exploiting CO_2 from humans/cattle. Several designs were evaluated, including bottle-based devices, Eave tube extension-based OHDs (Figure 7), fan-operated devices, and portable OHDs. The most effective stand-alone portable OHD consisted of the bottom half of a plastic bottle, covered with black PVC with a funnel-shaped netting extension to facilitate mosquito entry and trapping inside the device (Figure 7). A conical shaped cover was added to the device to create protection for the electrostatic netting treated with powder formulations of insecticides and facilitates downward channelling of the attractive odour lures placed inside the device. These prototypes were tested at different heights and locations and with independent sources of $CO_{2,}$ which is known to be important to boost attraction. Results varied, depending on the attractive odour blends deployed, but demonstrated that such simple portable and passive devices, even without additional carbon dioxide sources, have potential as OHDs to attract and kill host-seeking malaria vectors.

Fig. 7. *Left: Outdoor host-seeking prototype devices attached to eave tubes inside a semi-field system brick house. Right: bottom-entry design of a stand-alone OHD with conical cover.*

MCD semi-field tests

MCD prototypes were tested under ambient climate conditions in Tanzania. MCD attraction and mosquitocidal impacts were validated in semi-field screenhouses in Ifakara under controlled conditions (with known numbers of mosquitoes released and recaptured). Eave tube evaluations showed that tubes treated with insecticides were attractive to host-seeking females and significantly reduced overnight survival. On average, 80% of the released mosquitoes entered the Eave tubes, and bendiocarb-treated electrostatic netting killed 67% of these in a single night. We also conducted semi-field tests in western Kenya (ICIPE Mbita Point field station) to demonstrate the efficacy of Eave tubes in another environmental setting against different malaria mosquito strains and when deployed in a different house style (with mud walls and iron sheet roof; housing common in western Kenya). In these tests the final Eave tube insert prototype was evalauted (Figure 8). Results showed that on average more than 90% of *An. gambiae s.s*. and 76% of *An. arabiensis* mosquitoes entered the house through (open) Eave tubes each night, confirming their attraction. Eave tubes treated with deltamethrin reduced *An. gambiae* recapture rates with 70% overnight. These findings confirmed that eave tubes can kill large numbers of malaria mosquitoes approaching a house during a single night. Under field conditions and continuous deployment of tubes, the impact levels can be expected to be cumulative and even higher.

Fig. 8*. Experimental house inside the Kenyan semi-field screenhouse (A), indoor view of eave tubes (B), and insecticide-treated eave tube, view from outside the house (C).*

A novel video observation system to study the behaviour of mosquitoes inside eave tubes and measure actual contact times with the insecticide-treated netting inside the tube was developed. This video system was made from commercially available camcorders and used red LEDs as light sources (Figure 9). Semi-field video observation studies confirmed the attraction of Eave tubes, even when using insecticide-dusted electrostatic netting. Mosquito contact on bendiocarb eave tube netting was even lengthier than on clean netting; 95% of the mosquitoes filmed made more than 5 seconds contact, which is enough to transfer a lethal dose of insecticide.

Fig. 9. *LED light source (left) fitted on an eave tube with mounted GoPro camera (middle); experimental hut in semi-field system for video studies (right).*

These results indicate that insecticide-treated eave tubes are highly attractive to malaria mosquitoes and that they will pick up a lethal dose even in situations where they have the choice of flying out of the Eave tube. It is concluded that insecticide-treated eave tube netting can effectively reduce indoor mosquito densities and kill mosquitoes that attempt to enter through the tubes.

Fig. 10. *Smart Patch strip evaluated in semi-field tests in Tanzania.*

Smart Patch evaluations showed that for non-resistant vectors, patches made of LLIN material could significant boost the protective effect of an untreated bednet. A black netting Patch as small as 45 x 22.5 cm killed up to 62% of mosquitoes released overnight. In particular head-to-toe Smart Patch strips on the top (Figure 10) had a significant effect on the number of mosquitoes recaptured in the morning, and the proportion of recaptured mosquitoes that were bloodfed, indicating that they boosted the personal protection offered. Bendiocarb Smart Patches on top of insecticide-treated bednets were shown to impact the survival of pyrethroid-resistant mosquito strains. Results showed that the addition of bendiocarb-treated netting to the ceiling of a standard LLIN did not affect the proportion of mosquitoes able to take a bloodmeal but did significantly increase mosquito mortality rates. Because of their position and size, such additional Smart Patches may provide a feasible option to use actives that cannot otherwise be incorporated into bednets either because of cost, safety, or persistence constraints, and thus offer a promising new tool to respond to and manage the spread of insecticide resistance.

OHD studies in semi-field screenhouses showed that bottom entry traps were the most effective in attracting and killing malaria mosquitoes. OHDs with host-seeking blends added to slow-release granules consistently killed >90% of released mosquitoes and retained residual activity for 9 months. The efficacy of the optimised OHD containing both CO_2 and the “Mbita” odour blend was significantly higher than an OHD with either CO_2 or the blend alone. Most importantly, the efficacy of the optimised OHD containing attractive blends was shown to be significantly improved when incorporating granules with cyclopentanone. It appears that granules with cyclopentanone can substitute CO_2 in OHDs containing attractive blends, which is considered a major step forward in the development of passive stand-alone outdoor devices to control outdoor biting malaria vector populations.

MCD attractiveness and impacts under open field settings in Tanzania

Field studies were performed to assess the potential impact MCDs could have on malaria transmission. A large eave tube field trial was conducted in Mngeta, southern Tanzania. Mngeta consists of a rural conglomeration where 82% of the houses (with brick walls) were suitable for installation of eave tubes.

Fig. 11. *Installation of eave tubes in local houses in Mngeta, Tanzania. A local team of constructors was trained to render houses mosquito-proof, which includes sealing openings (at wall/roof level) with bricks/cement, screening windows with untreated netting, and installing eave tubes.*

In total, 1820 houses received the eave tube intervention, and 9157 eave tubes were installed; approximately 7 tubes per house (Figure 11). On average, 16.4 houses were finished each day. Training and operational activities were successful and showed that eave tube technology can be easily adopted in remote and rural settings. In the last stage of the intervention, coverage of 79% out of the 82% of houses being suitable for tube installation was achieved.

A social survey in Mngeta showed excellent community acceptance, with the majority of inhabitants considering the tubes effective and an improvement to their home. In total, 90% of the respondents were satisfied with the intervention and 71% noted a small or remarkable decline in the number of mosquitoes indoors after the intervention. Cost calculations showed that eave tubes will cost around 4 $ per person per year (Table 1) depending on house style and installation costs, which is more than 50% cheaper than indoor residual spraying (based on cost calculations from US-PMI). This indicates that wide-scale adoption of eave tubes should be feasible even in poorer regions where vector control is needed the most.

Table 1. *Eave tube costs/year for different house types, compared to currently used Indoor Residual Spraying.*

Total costs per year (in USD)	Traditional houses (open Eaves	Modern houses (closed Eaves)	Newly built houses	Indoor Residual Spraying (IRS)
Cost/area sprayed or tubes/yr	19,1	17,0	16,1	23,0
Cost per person per year	4,7	4,2	3,9	5,4

Our findings demonstrate that eave tube technology falls in a cost range that is competitive with existing malaria vector control interventions, which will allow for adoption even in poorer regions once WHO-recommendation has been obtained. The high coverage and community acceptance of this pilot rollout demonstrated that eave tube technology has the potential for wide-scale uptake at levels adequate to achieve significant impact and possibly community-wide effect similar to that observed when LLIN coverage is >80%. The fact that eave tubes can be significantly cheaper than IRS can help its chances of being taken up as a standard vector control method and possibly as a replacement method for IRS.

Smart Patch field evaluations in Ivory Coast showed that non-pyrethroid Smart Patches provided some personal protection via blood feeding inhibition and mortality, but not as much as LLINs. The level of protection from LLINs was considerably higher than expected in this area of insecticide resistance, which could have diluted Smart Patch impacts and raises the need for further field evaluations. Field trials with OHDs showed that light sources and skin odour blends are attractive cues for anopheline mosquitoes. Further optimisation of odour-release technologies and OHD designs will be needed to achieve low-cost products that can be effective at feasible levels of coverage. We did, however, deliver adequate proof-of-concept; showing that is possible to develop an effective stand-alone mosquito attraction device that does not require a power or carbon dioxide source.

MCDs in push-pull systems and integrated frameworks

The 'push-pull' approach*, i.e*. the use of deterrent stimuli to drive mosquitoes away from humans ('push') towards attractive devices ('pull'), was deployed to test the efficacy of our OHDs in combination with novel spatial repellents. We performed laboratory, semi-field and open field tests in Tanzania to determine the attractiveness of OHD prototypes in a push-pull framework at various levels of coverage. Catnip oil and the repellent component thereof (nepetalactone) were evaluated as push components. Repellent compounds were packaged in the slow-release system based on polymer granules inside a membrane pouch, and dispensed with electric fans. Room tests showed that catnip oil granules significantly decreased mosquito biting (on a volunteer) and significantly increased trap catches. In more realistic screenhouse settings, however, the use of catnip oil as a spatial repellent raised mosquito trap catches but biting rates were not lowered *(published in PLoS ONE: Obermayr et al., 2015).* Substances that block CO_2 perception were also evaluated, as these may augment the effect of spatial repellents by masking the presence of the most important host cue and potentially increase the chance of mosquitoes being captured by attractive devices.

We tested the four-component blend described by Turner *et al.* (2011) on the responses of *Aedes aegypti* towards CO_2 and skin odours in room tests. None of the treatments had an inhibitory effect and prevented mosquitoes from approaching the host. Even though these results show promise for OHDs to be used in push-pull frameworks, further optimisations will be required, in particular for long-lasting and effective repellent formulations, to ensure that OHDs will be effective enough and competitive with human hosts at realistic coverage levels.

To assess the potential impact of eave tubes in an integrated setting as projected for future implementation, they were tested in combination with bednets (LLINs) in a specially designed screenhouse; the so-called 'malaria village'. This system consisted of a large (30 x 20 m) compartment of a semi-field screenhouse with a miniature village of 6 houses and a viable mosquito population (Figure 12).

Fig. 12. *The 'malaria village', a simulated 6-house village in a 600 m² semi-field facility with an An. arabiensis population that was targeted by stacked interventions (LLINs and eave tubes).*

These 'malaria village' studies showed that stacked interventions of eave tubes and LLINs could virtually eliminate the screenhouse mosquito population. Whereas bednets managed to reduce the population density of anopheline mosquitoes (to an average of 32 mosquitoes captured per night), the addition of eave tubes almost completely eliminated the population (to an average of < 2 mosquitoes captured per night). These results demonstrate that eave tube technology has potential as part of an integrated vector management approach and can be used as a complementary tool in a background of bednet interventions.

Eave tube field demonstrations

To streamline field demonstration efforts, we engaged the World Health Organization to clarify which outputs were necessary to proceed towards eave tube product registration and product recommendation. Prototype MCDs were filed for WHO recommendation through the Vector Control Advisory Group (VCAG). The VCAG committee classified the eave tubes as being in late Phase 2 stage (out of a 3-stage process), and requested additional information, including field tests on house entry rated by wild-type species, and indoor comfort and air quality inside homes fitted with eave tubes. Field demonstration efforts therefore focused on accumulating this information via research in Tanzanian field tests instead of shifting activities to other regions or countries. As such, we focused on demonstrating attraction of eave tubes through video observations and showing that eave tubes do not negatively affect indoor climate (and thus comfort for house occupants). In addition, it was demonstrated that eave tubes may work cost-effectively in an integrated framework by modelling impact on malaria transmission based on actual parameters achieved from semi-field and field research outcomes.

We demonstrated Eave tube electrostatic netting impacts on multiple (insecticide-resistant) mosquito vector species in varying settings and climatic conditions. Using novel video monitoring technology, mosquito behaviour and duration of contact with netting in eave tubes was recorded and analysed to assess contamination with insecticides under open field conditions in Tanzania (Figure 13). We filmed 106 Individual wild type mosquitoes making contact with eave tube netting. Even with bendiocarb insecticide applied, we observed mosquitoes trying to enter; making proding movements, and making extended contact (on average 170 seconds) whilst sitting on the net. Behavioural analyses showed that 91% of mosquitoes made more than 5 seconds contact with the insecticide-treated electrostatic netting, which would result in a lethal contamination dose. These field-based video data demonstrated that eave tubes are attractive to host-seeking mosquitoes and that eave tube netting can achieve excellent contamination of mosquitoes with insecticides. Such visual proof of mosquito contact with an insecticidal surface is truly unique, since there are only few studies that demonstrate actual mosquito attraction and behaviour of mosquitoes to hosts under field conditions.

Fig. 13. *Videoing of wild mosquitoes entering the Eave tube and contacting the netting in Sagamaganga, Tanzania.*

Mosquito trapping studies in Tanzania served to demonstrate house entry by malaria mosquitoes prior to and after installation of eave tubes. Results from the test village Igombati demonstrated that the installation of tubes with untreated netting reduced indoor densities of malaria mosquitoes by >79% and *quinquefasciatus* (nuisance mosquito) densities by 44% (Figure 14). Collections in Mngeta village, where the large field trial took place, demonstrated that installing eaves tubes caused an average indoor mosquito density reduction of 75%. However, due to low population densities at the time of sampling, these results were not statistically significant. Compared to unmodified houses in a non-intervention area, eave tubes reduced indoor malaria mosquito densities by 84%. In houses that were not modified but were surrounded by houses that received eave tubes indoor densities also went down. These results provide compelling evidence that eave tube technology will be attractive to wild mosquitoes under tropical and rural/remote settings where effective malaria control is needed most urgently and that they may induce community-wide effects.

Fig. 14. *Mosquito trapping studies were done in unmodified houses with open eaves (left) and houses in which eaves were sealed and eave tubes were installed with either untreated or insecticide-treated netting (right). Eave tube installations resulted in large reductions in indoor numbers of mosquitoes.*

Studies were undertaken to evaluate the impact of eave tubes on indoor climate in a variety of house designs, during different seasons, and in various regions. Results showed that air replacement and ventilation in houses with open eaves is comparable to houses with eave tubes. Houses with corrugated iron sheet roofs had the most pronounced temperature fluctuations. After installation of tubes and closing other eave spaces, temperatures inside the house was slightly higher but comparable to those during the night (Figure 15). This means that for traditional houses with open eaves, instalment of eave tubes will not render the house less comfortable for inhabitants when indoors at night. It must be noted that in more modern house styles, the eaves are usually closed, and that installing Eave tubes would mean adding ventilation openings, which can be expected to actually improve the indoor climate via additional airflow.

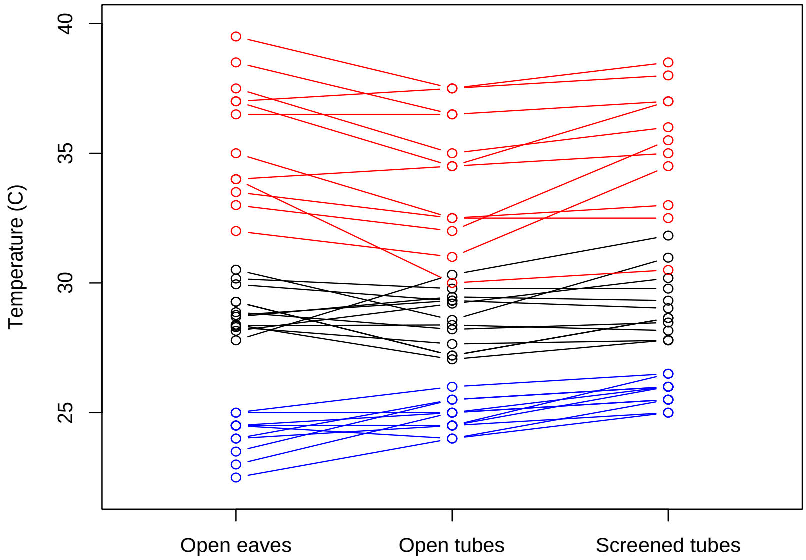

Fig. 15. *Daily minimum temperature (blue), daily average temperature (black) and daily maximum temperature (red) for Tanzanian houses with brick walls and iron roofs before modification (open eaves), after eave tube installation but without netting (open tubes) and after fitting netting with insecticide (screened tubes). Circles connected by lines represent individual houses.*

Using statistical mosquito feeding cycle models, parameterised by laboratory, experimental hut, and field studies, it was demonstrated that eave tube technology is likely to have a dramatic effect on malaria transmission by reducing infectious bites of mosquitoes. Even with low-level eave tube coverage there is likely a community level effect of this technology, so that even non-users will benefit from this intervention. Modelled impacts of eave tubes in combination with IRS (deployed in different houses) showed that combined use was the most effective approach to maximise the reduction in malaria transmission. In other words, the model outputs indicated that the best strategy would be to maximise eave tube coverage and use IRS in houses that are not suitable for tube installation. These modelling outcomes indicate the potential of MCDs in integrated malaria control frameworks and will be published in a peer-reviewed journal.

Potential impact, main dissemination activities and exploitation of results

Issues with current vector control

The mosquito vector control landscape has remained unchanged for decades, with only two widely used options at present: Long-lasting Insecticide Treated Bednets (LLINs) and Indoor Spraying with residual insecticides (IRS). LLINs in particular, of which some 1 billion were distributed in sub-Saharan Africa in the period 2000-2015 have contributed massively in averting close to 700 million cases and 6.2 million deaths during that same period[2]. Although optimism reigns, and global eradication of malaria is foreseen by 2040, there are several drawbacks with these tools:

- Resistance to pyrethroids, the only class of insecticides recommended by WHO for bednet impregnation, is spreading and intensifying rapidly;
- LLIN use is often low, particularly in hot and humid conditions, since it reduces airflow and thus comfort; nets also require daily deployment by users;
- IRS campaigns are forced to switch to more expensive carbamates or organophosphates due to high levels of pyrethroid resistance. Consequently, fewer houses can be sprayed with available budgets;
- IRS requires removal of household furniture, beddings, etc., which, combined with the stains on walls and smell of insecticide application frequently leads to refusals by house owners to have their houses sprayed.

In conclusion, resistance to insecticides has dramatically increased the cost, and consumer usage and acceptance of the two approaches is far from optimal. This is why the MCD project Consortium focused on novel yet low-cost and user-friendly technologies that could complement existing vector control tools and be deployed even in resource-poor settings where malaria is causing severe human health issues.

MCD impacts on vector control

The electrostatic coating technology was shown to have resistance-breaking potential and can support the use of new insecticide classes or combinations thereof. Electrostatic netting applications offer opportunities for deploying resistance-breaking actives in mosquito control tools such as the Eave Tubes. With growing problems with insecticide resistance in many developing countries, this technology could provide a significant step forward in malaria vector control and resistance management.

We successfully developed 3 different MCD prototypes, of which 2 were advanced to proof-of-concept stage and one was developed from idea to production-ready and subsequently field-validated. Smart Patches show promise as a cost-effective tool to augment bednet efficacy against (resistant) mosquitoes. Bednet manufacturers have expressed interest in this novel technology, in particular as a means to apply novel resistance-breaking chemistries. OHD prototypes proved that

[2] Bhatt, S. *et al.* (2015). *Nature*, 2015 Sep 16. doi: 10.1038/nature15535. [Epub ahead of print]

stand-alone devices can successfully attract and kill malaria vectors and show potential for use in future push-pull frameworks.

The most advanced MCD, the Eave tube, is a game-changing household protection product that leverages the natural route of malaria mosquitoes into houses and provides a low-cost and safe option to kill them with insecticides. Eave tubes operate passively, i.e. do not need repeated actions from house owners as is the case for bednets. Eave tube technology renders the house mosquito-proof and reduces indoor mosquito densities significantly. Eave tubes require only a fraction (<5%) of the insecticides used on LLINs or in IRS as only small pieces of netting are treated. Therefore, enormous reduction in insecticides (>95%) can be achieved, which greatly reduces the costs and environmental impact of this intervention. Also, being at eave height, netting is out of reach of house occupants, which enables the use of novel (resistance-breaking) chemistries and making this product a very safe vector control option.

The MCD studies demonstrated that Eave tubes could be used as a complementary product in integrated control frameworks. Eave tubes were shown to boost the impact of LLINs and can help suppress mosquito populations to a level where malaria transmission will practically cease altogether. Even though Eave tubes are competitive in efficacy, durability and cost, IRS can still provide an additional benefit as models showed that deploying IRS in houses that are not suitable for Eave tube installation would be an ideal combination with the highest possible impact on malaria transmission.

Impact on malaria control

Malaria is endemic in 106 countries worldwide and infects more than 200 million people each year. Approximately 81% of these cases originate from the African region and 13% from the Southeast Asian region. The disease remains a substantial public health problem with an estimated 438,000 deaths in 2015; mostly children and pregnant women. Malaria also remains a serious health risk for travellers and disproportionately affects children under the age of five and the rural poor. Transmission intensity in rural areas is nearly always higher than in urban areas. Particularly in remote resource-poor areas people do not have access to appropriate healthcare and often cannot afford a bednet for prevention. These concerns emphasise the need for low-cost tools that can be used in rural settings to complement current interventions.

Eave tubes are now considered as a potent additional tool in the vector control toolbox that can benefit human health by reducing and preventing malaria transmission, cutting down the number of episodes and limiting the severity of this disease. Eave tube technology can provide a solution to current malaria control problems encountered with resistance, user acceptance and increasing vector control costs since it is highly, resistance-breaking, user-friendly, safe and cost-competitive. Eave tubes provide household level protection, which is a massive step forward compared to the temporary and personal protection provided by bednets. We consider it a significant step forward to be able to protect the most vulnerable groups (children below the age of five and pregnant women) that suffer mostly from malaria.

Novel tools like eave tubes will be needed to eliminate malaria in some of the hardest hit parts of the world. It is known that bednet use can drop sharply when malaria transmission ceases (temporarily). Eave tubes provide a cost-efficient passive vector control technology that can be continuously deployed and can contribute in keeping malaria-free areas void of recurring transmission. Our goal is to proceed with epidemiological impact trials and commercialisation of eave tubes to ensure that this intervention will come to full fruition and be adopted on a wide scale to generate maximum impact on malaria transmission.

Impact on non-malaria mosquitoes and agricultural insect pests

Our novel application technology, i.e. electrostatic coating applications of insect-killing bioactives, has great promise for deployment in other areas of public health and economic importance, including neglected tropical disease control and agricultural pest management. Electrostatic netting is already being deployed in point-source contamination traps against Dengue vectors, using novel combinations of biological actives and autodisseminants. As shown and published in *PNAS*, the electrostatic coating technology can boost insecticidal impacts, reduce application doses, and expand options for using multiple bioactives and mixtures, which is a significant step forward in the field of insect pest control wherever issues with insecticide resistance are causing problems.

Eave tubes have potential to not only reduce densities and biting rates of malaria mosquitoes but also other nuisance and disease-carrying mosquitoes, which are often present in much higher abundance. We showed that Eave tubes successfully attract *Culex* mosquitoes and that the electrostatic netting can effectively kill (insecticide-resistant) culicine and aedine mosquito species. Eave tubes can thus minimize the risk of contracting other health-threatening mosquito-borne diseases like lymphatic filariasis, dengue fever and Chikungunya. These illnesses can cause severe economic impacts in endemic countries, and the provision of a new and effective control tool may help alleviate the health costs and economic burdens they impede.

Socio-economic impacts

Our successful Eave tube rollout in close to two thousand houses in Mngeta (rural Tanzania) delivered a significant impact on the local community; we managed to deploy Eave tubes in almost 80% of the houses and protect on average 10.000 inhabitants from malaria mosquitoes for more than 1 year during the MCD project period. At present, IHI has taken full responsibility for the upkeep and re-treatment of eave tube nettings and as such will serve as the direct contact point for the community. This field trial demonstrated that eave tube technology has the potential for wide-scale uptake at coverage levels adequate to achieve significant impact and possibly community-wide effects on the malaria vector population. We showed that houses that do not receive the eave tube intervention will still benefit from the presence of tubes elsewhere since mosquitoes are not merely deflected from houses but actually killed when they try to enter.

We explored the preferences of local inhabitants for anti-mosquito technology and what it would take to gain acceptance of eave tube technology. Social scientists within IHI's demographic surveillance system were actively engaged and carried out a KAP questionnaire study in this rural community. The outcomes of this social survey obtained valuable insights on the perception and attitude towards eave tubes and their impact on mosquitoes and malaria. Results showed that user acceptance exceeded 90%. Inhabitants perceived eave tubes as an improvement of their home and felt protected from mosquito bites and malaria. The fact that coverage and community acceptance was already this high, even without active community sensitisation, shows that eave tube technology has great potential for broad uptake across Africa.

Cost calculations showed that eave tubes can be significantly (50-60%) cheaper than IRS, which will help its chances of being taken up as a malaria vector control method. Through design and production process developments, eave tubes are ready for mass production and commercialisation. The light-weight and stackable gauze inserts can easily be removed from the tubes, retreated and replaced when needed, which enables cost-efficient large-scale deployment. Since there are not many alternatives to pyrethroids offered or new tools already commercially available, we foresee that eave tubes can be interesting to the pest control market and not only be deployed via donor-funded implementation but also through commercial channels and direct sales to consumers.

In future, eave tube deployment may provide economic benefits to local communities and become an important new source of employment. Local industries can be engaged in the manufacturing of tubes and inserts, and local people can be involved in their distribution, sales, installation, and servicing. Effective malaria control will benefit economic growth and improve the living conditions of people in malaria-endemic areas. Less malaria means less impairment of cognitive abilities in children and less absenteeism from school. The living standard of local households will improve because fewer workdays are lost and productivity will increase due to absence of illness. Studies have shown that in malaria-endemic countries large parts of the household budget are spent on healthcare and prevention measures, which can be reduced or saved when control becomes more effective. By providing protection from malaria we may help render impoverished populations better capable of protecting themselves through higher income and better access to healthcare, which can lead to an upward spiral of well-being, living conditions, and development at large.

MCD Project External Advisory Board

To ensure good uptake of the results and close contact with potential stakeholders, the MCD Project had an External Advisory Board (EAB) consisting of researchers and other stakeholders that provided useful feedback on results over the course of the project. At the start of the project, the EAB consisted of 5 experts with scientific knowledge in malaria/mosquito research. Later on, experts with more industrial skills (e.g. production, distribution, marketing) or field operational experience were included so that the board broadly represented potential MCD stakeholders. Through this interactive approach exploitation of the project's results was maximised. Members of the EAB actively participated during the annual progress meetings when results were presented and discussed, and provided valuable feedback on MCD developments, exploitation options and market entry strategies.

Dissemination activities

The MCD project used various dissemination channels and materials to reach its identified target groups and stakeholders. Several local and international events/conferences were attended and the MCD project members also extensively used the press as a channel to disseminate project outcomes, including local and international media via science journalists and the mainstream press.

THE MCD PROJECT

An MCD project logo was designed in the first months of the project. General information about the project and its aims and achievements was presented to the public at large in the publicly accessible part of the MCD project website: http://www.mcdproject.org. News items, partner profiles, relevant contact details, public project deliverables, notifications and downloadable brochures were regularly posted on this website.

MCD project research outcomes were disseminated via publications in scientific journals that have broad readership and high impact. In total, 5 articles were published in Open Access peer-reviewed academic journals within the project period. Two of these were published in prestigious high impact journals; the Proceedings of the National Academy of Sciences USA (PNAS) and the Public Library of Science (PLoS ONE). The PNAS publication received much attention since it also featured on the journal cover. Nine more manuscripts are being prepared for publication, which will be submitted within the next few months. These will include a series of six manuscripts on the eave tube technology, which is now being compiled by the MCD team.

Over the course of the Project, MCD Consortium staff attended a large number of events. Several scientific presentations were given during meetings, seminars and (international) academic conferences. These included keynote presentations at high profile meetings (e.g. Keystone symposia (Mexico), Society of Vector Ecology (Greece), the Royal Society of Tropical Medicine (UK) and the Leopoldina Academy of Sciences (Germany). Several academic conferences and public health events were visited to disseminate MCD project results. For instance, BG, IHI and I2C project senior staff members participated and presented progress during the 6th MIM conference in Durban, South Africa (October 2013). In November 2013, PSU was invited to take part in a landscaping meeting organized by the Bill & Melinda Gates Foundation during the annual ASTMH meeting in Washington DC and presented the Consortium's work there.

The MCD project received much attention from local and international media. Project results and progress were presented to various news sources and a variety of media outlets (e.g. social media), television and newspapers. Each of the consortium members utilised their own channels to reach both national and international news sources. In2Care had a series of articles published in a major Dutch newspaper. It also issued a press release in January 2014 and was, together with BG, able to showcase activities to the press during the EU Innovation Convention in Brussels (March 2014). The MCD project was listed on the EU website as a success story by EU Horizon 2020 news reporters. On 3 June 2014, the EU publicised the feature article that details the successes of the project to date. Subsequently, a Dutch TV channel (Nieuwsuur) produced a 13-minute documentary on eave tubes that included an interview with the Project Officer and was broadcasted on 19 July 2014. In June 2015, the 'eave tube' concept developed by the MCD project featured in a short movie sponsored by the Dutch company DSM as part of their 'science can change the world campaign'. This film has reached close to 5 million viewers in less than 6 months and was followed by an additional short movie about eave tubes.

Eave Tube and Smart Patch prototypes were evaluated in several locations and were shown to representatives of beneficiaries, stakeholders and potential investors like industrial manufacturers, donor communities and end user groups. Demonstrations in Kenya, South Africa and Ivory Coast served to show the applicability of eave tubes and Smart Patches in various malaria-endemic settings. The Kenya work in particular served as a formal introduction of the final eave tube product outside Tanzania. MCD prototypes were showcased in several academic meetings, not only to generate interest but also to discuss their workings and underlying principles that may be of value in academic research and (agricultural) pest control. Several outreach meetings with important stakeholders were organised, including the Gates-funded Innovative Vector Control Consortium (IVCC, Liverpool, UK), the Tanzanian company A-Z Textile Mills Ltd., the World Health Organization (WHO), Doctors without Borders (MSF), and the Swiss Tropical and Public Health Institute (STPH). Contact was established with the US President's Malaria Initiative's technical advisory partner (CDC, Atlanta) and eave tube technology was presented in detail to responsible staff to garner support and technical input as well as identify possible means to obtain operational research funding from US-PMI. I2C has had discussions with Dr. Walter Seidel from EU Devco to see if funds could be available for large rollouts parallel to the RCT trial in West-Africa that could help progress eave tube uptake in several countries.

Exploitation of foreground

Foreground IP generated during the project was protected by filing a joint patent on the novel MCD prototypes that were invented and discussed during the first project meeting. This patent is titled: *A complex of structures for delivering pesticidal agents to arthropods* and was filed in October 2013 under the application number 13187690.6 - 1656 (Ref. no: 50.1224 EP). Following review, claims had to be re-drafted and re-submission took place in October 2015. The project also yielded exploitable foreground that was not patented and consisted of scientific discoveries and general advances. Several of these hold potential for commercialisation, other advances will merely benefit the broader (scientific) community and have been or will be made available in the public domain through scientific publication.

IPR agreements were made and specified in the Dissemination & Exploitation Plan. MCD consortium members agreed that all background IP shall remain with the respective owner but may be used on a royalty-free basis for the duration of the project and afterwards through material transfer agreements (MTA) or licensing and royalty-free use for R&D purposes only. For foreground intellectual property, specific agreements on ownership, access rights, licensing and protection measures were made and endorsed by all Consortium partner institutions.

Further financing and projects

Several project proposals were drafted and submitted to funding organisations to further MCD technologies. PSU and I2C were invited in May 2015 by the Bill & Melinda Gates Foundation (BMGF) to submit a proposal, which was granted in November 2015. The BMGF grant funds two major components: A large cluster randomised controlled trial (RCT) with epidemiological outputs in Ivory Coast (where pyrethroid resistance levels are high), and commercialisation activities such as market research and implementation pilots to facilitate product uptake at the end of the grant in Tanzania. The RCT will encompass a study of 20 control and 20 treatment villages in Ivory Coast in which a maximum of 60.000 eave tubes will be installed. Together with the London School of Tropical Medicine and Hygiene (UK) and the Institute Pierre Richet (Ivory Coast) impacts on mosquito populations and malaria incidence will be studied over a 3-year period. The aim is to successfully complete step 3 in the WHO/VCAG process and move towards WHOPES recommendation for the eave tube as an established malaria vector control tool. From the 3rd year onwards, implementation pilots will start in several locations in sub-Saharan Africa to explore routes-to-market and develop a business plan to commercialize eave tubes successfully by the end of this 5-year project.

IHI and I2C jointly developed a proposal for the UKAid funded HDIF initiative, which was submitted in November 2014. This project was awarded in February 2015 and focuses on the implementation of eave tube technology in 2000 houses in peri-urban settings in Tanzania (Dar es Salaam and Morogoro). Funds are also available to initiate commercial-scale production of eave tubes, and this activity is currently underway.

Address of the project public website and contact details

MCD poject website address: www.mcdproject.eu

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