The Potential Role of Aerial Spraying for Malaria Elimination: A Technical Note

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The **Malaria Elimination Initiative (MEI)** at the University of California San Francisco (UCSF) Global Health Group believes a malaria-free world is possible within a generation. As a forward-thinking partner to malaria-eliminating countries and regions, the MEI generates evidence, develops new tools and approaches, disseminates experiences, and builds consensus to shrink the malaria map. With support from the MEI's highly-skilled team, countries around the world are actively working to eliminate malaria—a goal that nearly 30 countries will achieve by 2020.

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Background

Significant progress has been made in the last decade in reducing malaria transmission around the world. Numerous and ambitious malaria elimination goals have been set at the national and regional levels with a recent call for malaria eradication by 2040.[1] With near-term malaria elimination targets approaching, countries are working to optimize and scale existing interventions, but in many places, more aggressive approaches will be needed to achieve zero transmission, including new drug-based approaches to target parasites in humans and new or underutilized vector control approaches to target mosquito populations and reduce human-vector contact.

While insecticide treated nets (ITNs) and indoor residual spraying (IRS) remain the backbone of vector control for malaria elimination having achieved significant impact to date, there is a limit to what they can achieve: evasive mosquito behaviors lead to outdoor and early biting, operational inefficiencies yield low effective coverage, and insecticide resistance is emerging as a potential threat to the sustainability of these interventions.[2] To meet elimination and eradication targets, there has been a call for innovative and aggressive vector control interventions to supplement ITNs and IRS to 'close the residual transmission gap'.[1] National malaria control and elimination programs urgently need access to supplementary VCTs and innovative delivery mechanisms.

Building on the vision of the UCSF Global Health Group's Malaria Elimination Initiative (MEI) through its collaboration with the Parker Foundation to identify transformative approaches to malaria vector control, the MEI explored mosquito control programs in high resource settings to identify best practices for application to lower resource, malaria endemic countries through a series of case studies on mosquito control, including Australia and the United States. As recognized by the MEI and Parker Foundation, aerial application of insecticides is common in these countries to control nuisance and vector mosquitoes. How has aerial spraying been used in the past across high and low resource settings and how is it used today? What is the technical guidance for aerial spraying and is there infrastructure to support its application in low resource settings? What is the potential of aerial spraying as part of more innovative and aggressive malaria elimination strategies?

Aircraft have been used since the 1920s in the US and for decades in other high resource settings (e.g. Australia, Japan, and Germany) to control disease vectors and agricultural pests, including *Anopheles* mosquito populations. Aerial delivery of DDT and other insecticides was a component of several malaria elimination programs around the world during the Global Malaria Eradication Program of the mid-20th century. Despite this long history, there is a dearth of evidence on the impact of aerial insecticide application on malaria transmission, leading to limited use in malaria endemic areas. Aerial infrastructure, including fleets of aircraft, pilots and maintenance teams, and spray technology exists across Africa, the Asia-Pacific, and Latin America and can be leveraged and repurposed for *Anopheles* control. Eliminating countries need ready solutions to drive down transmission, and testing out aerial approaches in real-time will expand the evidence base while potentially having a dramatic impact on mosquito populations and mosquito-borne disease.

Here we summarize the usage history and available evidence of aerial spraying for both larviciding and adulticiding, and explore the various technical and logistic considerations for successful aerial control.

Aerial Larviciding

Larviciding is the regular application of biological or chemical insecticides to water bodies. Unlike ITNs and IRS, which target adult mosquitoes, larviciding offers a different mode of action by targeting the immature, aquatic stages of the mosquito (the larvae and pupae), thereby reducing the abundance of adult mosquitoes.[3] Ground-based larviciding, by vehicle or manually using backpack sprayers, is most commonly used since it enables direct targeting of larvicide to larval habitats. The evidence on effectiveness of ground-based larviciding for malaria in both high and low income settings is well-established, and recent normative guidance and policy recommendations for larviciding for malaria have prompted scale up in malaria-endemic areas.[3] In a recent Cochrane Review on larval source management (LSM), larviciding alone was shown to reduce malaria incidence by 74% in two cluster-randomized controlled trials (RCTs) and reduced parasite prevalence by 90% in a cluster-RCT, all undertaken in Sri Lanka.[4] However, ground-based application can be impractical and resource intensive in large-scale areas or when larval habitats are difficult to reach. Despite limited evidence on the effectiveness of aerial larviciding on malaria transmission, anecdotal and operational evidence exists on its impact on disease transmission and mosquito population control. Aerial larviciding can provide an alternative delivery mechanism for use in settings such as rice fields or wetlands, or in areas where there are cryptic larval habitats only findable and reachable by air.

Aerial larviciding for mosquito control has been utilized for decades as an important tool by many programs in high resource settings, notably the US, Australia, and Germany. The primary focus of these applications is to control nuisance mosquitoes, particularly floodwater species, as opposed to disease vectors. In the US, aerial larviciding is conducted by most states, primarily under the management of a local government vector control organization. In some areas, Florida being the leading example, the local government programs own the aircraft that are used specifically for insecticide delivery of both larviciding and adulticiding. In many other states, aerial larviciding is conducted by private aerial application contractors, whose primary business is spraying for agricultural or forest pests; therefore, the aircraft are specifically designed and equipped for insecticide delivery. Multiple mosquito species can be targeted in a variety of habitats, requiring a thorough understanding of species behavior as well as rigorous larval surveillance.

In Germany, the German Mosquito Control Association (KABS) efforts are focused on the Rhine River's flood plain, primarily by larviciding with Bacillus thuringiensis israelensis (Bti), a bacterial larvicide that interrupts larval feeding. Through aerial distribution of a granule Bti formulation targeting dense vegetative canopy along the Rhine, KABS achieved 91–98% larval mortality rates in field tests.[5] The impact of aerial larviciding in controlling mosquito populations has also been demonstrated in New Zealand. In the 1990s, Aedes camptorhynchus, an invasive southern saltmarsh mosquito, migrated from Australia to Hawke's Bay, New Zealand, and quickly spread to ten other sites on the North Island. In response, academic and operational experts from the Australian mosquito control community developed an eradication strategy centered on aerial larviciding.[6] Within 15 years, the team was able to successfully eradicate *Ae. camptorhynchus* from New Zealand.[7] When larval measures are insufficient alone, these mosquito control programs often add adulticiding measures.

Aerial Adulticiding

Adulticiding refers to the use of insecticides to rapidly reduce adult mosquito populations.[8] Adulticiding is generally undertaken in these high resource settings when larval control measures are insufficient or not feasible, often following a significant increase in mosquitoes or evidence of a mosquito-borne disease.

The most common method of adulticiding is ultra-low volume (ULV) spraying (i.e. space spraying), which is the process of applying very small amounts of liquid into the air as a fine mist of droplets. These droplets float on the air currents and eliminate mosquitoes that come into contact with them. Adulticides can be applied from hand-held sprayers, truck-mounted sprayers, helicopters, or airplanes.

Aerial ULV adulticiding has been practiced globally for decades to control mosquitoes and disease transmission. Recently, an aerial adulticiding campaign was undertaken in California following an upsurge in West Nile Virus (WNV) in 2005, resulting in 779 human cases and 28 deaths. Treatment consisted of a single application of a pyrethrin insecticide applied as a space spray covering an area of approximately 1.2 million acres, or over 1,800 mi2. Following this intervention, no new cases of WNV were reported in the treated area, and analyses indicated aerial spraying had significantly reduced the likelihood of transmission six-fold compared to untreated control areas.[9] In 2007, a similar study was conducted to address a WNV outbreak in Sacramento and Yolo districts, also in California. The study targeted *Culex tarsalis* and *Culex pipiens* species, mosquito vectors of WNV, across 53,000 acres.[10] Pre-treatment infection rates reached up to 10.85 and 7.87 per 1,000 mosquitoes for *Cx. tarsalis* and *Cx. pipiens*, respectively with the recording of the first human cases triggering the aerial intervention. Following a single aerial treatment, results demonstrated a significant reduction in the abundance of the target species (57% for *Cx. tarsalis*; 41% reduction for *Cx. pipiens*) and in the infection rate of *Cx. tarsalis* to 3.42 per 1,000 mosquitoes.

Outside the US, there is evidence of aerial adulticiding to control disease transmission in Thailand, Brazil, Tanzania, and Haiti. In 1968, aerial spraying of the insecticide malathion were successfully applied to control an upsurge of Aedes aegypti causing dengue outbreaks in Thailand. A large-scale trial conducted in Nakthon Sawan, Thailand, across over 4,000 acres including parts of the city, reported reduction in landing rates of 95% and 98% following two sequential spray applications, and overall reductions in trap collections of between 88–99% ten days post-treatment.[11] In this study, only 8% of remaining female mosquitoes collected post-treatment were infected with dengue, compared to 30% of the population pre-treatment. A similar trial of malathion by aerial application was conducted in Brazil in 1975 against *Aedes* to control an arbovirus on the coastal areas south of Sao Paulo and reported similar rates in mosquito population reduction.[12]

While there is limited evidence on aerial adulticiding for malaria control, one example in the literature is of aerial application of malathion to control malaria transmission in Miragoane Valley of Haiti during an epidemic of *Plasmodium falciparum* in the 1970s.[13] Aerial spraying was used as a supplement to ground-based adulticiding, resulting in a significant drop in mosquito density and a reduction in malaria cases four weeks following treatment. Over a three month period, the number of malaria cases decreased from 180 per 10,000 of population per month during the peak transmission period, to around 16 cases per 10,000 in sprayed areas, compared to 64 cases per 10,000 in unsprayed areas over the same period, a reduction in malaria incidence of 75%.

The only documented attempt of aerial adulticiding to control for *Anopheles* mosquitoes in Africa identified for this report was in Tanzania in 1958 using granules of dieldrin.[14] This trial coincided with the adoption of IRS with DDT which had a significant impact on malaria transmission at the time, thus making aerial spraying less favorable. Since then, no further trials on aerial adulticiding for malaria control have been carried out in Africa to the best of the authors' knowledge.

Aerial Spraying to Control Non-mosquito Disease Vectors in Africa

Despite limited evidence on aerial application for *Anopheles* control, aerial larviciding and adulticiding have been successfully employed to control or eradicate vectors that transmit other vector-borne diseases in Africa. This existing capacity and technology for aerial spraying can be repurposed for malaria elimination and valuable lessons from these experiences can inform operations moving forward.

Onchocerciasis, or river blindness, is a neglected tropical disease caused by a parasite transmitted through the bite of an infectious blackfly and can result in blindness.[15] In the 1970s, the Onchocerciasis Control Progamme (OCP) in West Africa successfully employed aerial larviciding to help break the life-cycle of the parasite through eradication of the blackfly vector. OCP conducted aerial larviciding campaigns with Bti over rivers and streams, the breeding sites of blackflies.[16] The first aerial larviciding treatments began in areas with the highest incidence of onchocerciasis and eventually expanded to cover over 250,000 mi2 spreading over seven countries: Burkina Faso, southeastern Mali, southwestern Niger, northern Cote d'Ivoire, Benin, Ghana, and Togo.[17] Following 14 years of consistent spraying, combined with treatment of eligible populations with ivermectin, the program was able to interrupt local onchocerciasis transmission.

Since the 1950s, wide-area aerial adulticiding has been used to eradicate tsetse flies in Africa with significant success. Tsetse flies transmit Trypanosomiasis, also called African sleeping sickness; the effects of Trypanosomiasis on human life and the economy of Africa are devastating, claiming 55,000 human lives and 3 million cattle each year, and resulting in economic losses of $4.5 billion annually.[18] From 2000 to 2014, successful programs have been undertaken in Ghana,[19] Botswana,[20] Zambia, Burkina Faso, Ethiopia, Namibia, and Angola (Table 1). Eradication of tsetse flies can be attributed to aerial spraying as part of an integrated vector control approach supplementing other strategies, which include the use of odor attract-and-kill mechanisms and treating cattle with endectocides, or anti-parasitic treatments. The aerial program used manned aircraft for 4–5 weekly spray applications treating up to 7,700 mi2 each application, timed to coincide with emerging adult tsetse flies. Aerial application has been cited as one of the most effective control strategies against tsetse flies since it operates at such a large scale.[2]

Table 1. African aerial tsetse control (Orsmond Aviation, South Africa)

Country for Tsetse fly control	Year	Per spray (area mi2)	Total coverage for year (sequential area mi2)
Botswana	2001	4,430	22,145
Botswana	2001	5,320	26,595
Botswana, Namibia, Angola, Zambia	2006	6,215	31,070
Angola & Zambia	2009	6,215	31,070
Ghana & Burkina Faso	2010	5,400	31,070
Ethiopia	2012	3,110	21,575
Zambia	2014	3,915	12,430

Technical Considerations

Given the operational and financial requirements for larviciding and adulticiding, it is important that ministries of health considering the use of aerial spraying for malaria elimination assess the entomological and epidemiological impact, operational feasibility, cost-efficiency, and regulatory requirements for aerial spraying compared to current interventions and ground-based applications. Additional factors must be considered to ensure successful implementation of aerial campaigns. First, ecology, weather, and the timing and frequency of application must be optimal for successful application. Second, understanding the advantages and disadvantages of the different types and formulations of larvicides and adulticides will increase the effectiveness of the application. Finally, the type of aircraft and technology utilized is central to optimizing aerial applications and achieving the desired impact.

Meteorology, Timing, and Ecology

Meteorological conditions and timing of application are not as critical for larviciding as compared to adulticiding. When applied as a solid granule (the most common formulation), larvicide tends to fall rapidly to the ground and is very minimally affected by wind and rain. However, if liquid formulations of larvicide are used, flight height and droplet size are important factors to consider for preventing the displacement of spray applications by wind conditions. Furthermore, the fall time of liquid larvicide droplets will be determined by evaporation rates, which are influenced by ambient air temperature, relative humidity, and liquid properties. Aerial larviciding can be conducted at any time of the day since larvae are stationary within their habitat.

For aerial ULV adulticiding, which involves much smaller droplets (around 10–40µm), the prevailing wind conditions can carry spray material over great distances and droplets will fall in a more horizontal trajectory. Thus, ideal spray conditions involve stable air and a temperature inversion (in which temperature increases with altitude) so that droplets will not be carried upwards in strong convective currents. These conditions tend to only occur in early morning or late evening, which generally coincides with the periods when adult mosquitoes are most active especially for *Anopheles*, although this varies by location and target species. Aerial adulticiding campaigns are usually conducted at night at low altitude in order to maximize target coverage, risky conditions that require highly skilled pilots. Also critical to success is ensuring sequential applications made over short time frames with appropriate intervals between applications (e.g. a few days apart).

Insecticide

Selecting the appropriate insecticide formulation is critical to the success of control efforts. The decision on which larvicide formulation is most appropriate for mosquito control is based on habitat features: variables such as type, height, and density of vegetation determine whether liquid or solid larvicide will be most likely to reach the target habitat or combination of habitats being treated. Liquid larvicides are diluted in water and applied through a spray system, whereas solid formulations combine larvicide with sand, clay, or corn cob granules and are applied through a spreader system. Liquid formulations tend to be less expensive and more efficient in terms of coverage due to wider operational swath widths when utilizing low-volume to ultra-low-volume application techniques. However, unlike ground-based applications that are made directly to the larval habitat, aerially applied larvicides often have to pass through vegetative canopies to reach the water containing mosquito larvae below. Since these canopies can intercept a good portion of the spray droplets, preventing them from reaching the larval habitats, solid formulations of larvicide tend to be more efficient as mentioned above. There are five main groups of larvicides: oils and surface agents, synthetic organic chemicals, bacterial larvicides, spinosyns, and insect growth regulators. Of these groups, only certain products have been approved by the World Health Organization Pesticide Evaluation Scheme (WHOPES) as safe, stable, potent, and efficacious.[3]

Adulticide choice is based on several factors including efficacy, mosquito species susceptibility, safety, and cost. To avoid contact with non-target organisms, such as bees and butterflies, applications are timed to coincide with mosquito flight activity. Common insecticides used for aerial adulticiding include malathion, naled, chlorpyrifos, permethrin, resmethrin, and sumithrin.[22]

In areas of increasing insecticide resistance, especially to pyrethroids, national malaria programs must select insecticides for adulticiding cautiously and based on local evidence on insecticide susceptibility.

Aircraft

Aerial applications of larvicide and adulticide can be conducted by either fixed wing or rotary aircraft (i.e. helicopters) (Table 2). Both types of aircraft are suitable for solid and liquid formulations of larvicide, as well as ULV adulticide spraying. Aircraft can be adapted by a variety of hoppers, nozzles, and metering systems, allowing the same craft to be used for both larviciding and adulticiding. Most aircraft in the US are fixed wing since they have a reasonable payload, are moderately fast, economical to operate, and practical to maintain, although use of helicopters is increasing.[22] Helicopters have the advantage of tighter turns and more maneuverability but are more expensive than fixed wing aircraft. Meteorological conditions must also be considered when selecting aircraft, regardless of whether larviciding or adulticiding is being conducted. Larger aircraft are less likely to be affected by wind conditions, but smaller aircraft are limited to light wind conditions (i.e. less than ~10mph wind).

In the US, mosquito control districts have varying operational models for fleet ownership: some purchase aircraft and employ a pilot and maintenance crew while others contract these services from private aerial applicators. It is common for districts to rent such equipment, as well as the aircraft and pilot time, from agricultural flying services, allowing districts to avoid expenses for in-house maintenance and staff.[22]

Increasingly gaining popularity for vector control and surveillance, unmanned aerial vehicles (UAVs) offer a promising alternative to manned aircrafts in specific settings. UAVs were first investigated for use in agriculture and forestry in the late 1970s. In recent years, advances in technology have led to enormous interest in UAVs for vector and pest control, both for remote sensing and application of insecticides. In Japan, for example, UAVs are used to control pests in over 60% of the agricultural settings. UAVs may be advantageous to manned aircraft in more spatially selective applications for targeting villages or small areas with larvicides, and in some cases, adulticides. UAVs can be operated with very limited resources and do not require complex infrastructure. However, the productivity of UAVs is less than manned aircraft (e.g. payload capacity is less, flight distances are shorter; Table 2) and there are significant regulatory hurdles to consider, along with unanswered questions around the impact of UAV insecticide delivery on mosquitoes and malaria.

Table 2. Productivity of spray aircraft

				Adulticides		Larvicides	
Type of aircraft	**Capacity (gallons)**	**Flight time**	**Speed (mph)**	**Spray time**	**Area (acre)**	**Spray time**	**Area (acre)**
Multi engine aircraft	520–1320	6 hrs+	125+	1–3 hrs	25K–50K	n/a	n/a
Twin engine	13–520	4 hrs+	125+	1–2 hrs	25K–37K	15–60min	600–2500
Fixed Wing–Turbine	390–650	4 hrs+	125+	1–2 hrs	25K–37K	30–60min	750–3100
Fixed Wing–Piston	195–390	4 hrs+	90+	1–2 hrs	18.5K–30K	30–60min	370–1900
Helicopter	13–260	4 hrs+	30–60	1 hr	6K–12K	20min–2hr	300–1250
Ultralight	13–26	4 hrs+	30–60	20–40min	1k–2k	5–40min	30–125
UAV < 220 lb	13	1hr	30	15–20 min	745	20–40min	30–65
UAV < 45 lb	2.5	30 min	20	5–10 min	185	10–20min	3–12
UAV < 20 lb	1.5	20 min	20	5–10 min	100	5–10min	1.5–3
UAV < 10 lb	0.5	20 min	20	2–4 min	37	2–4mins	0.75–1.5

Infrastructure

The infrastructure for aerial application exists in many malaria-endemic parts of the world and simply needs to be repurposed for *Anopheles* control. In sub-Saharan Africa, where 90% of the world's malaria cases occur, there are an estimated 200 manned aircraft equipped for aerial spraying, many of which are already used for ULV applications (Table 3). This is equivalent to the size of the aircraft fleet engaged in the US for mosquito control. Of these 200 aircraft, about half are located in South Africa or neighboring countries that are at the front line of malaria elimination. Some aircraft are currently dedicated for agricultural spraying, while others are military aircraft that can be deployed for emergency pest control programs. As practiced in the US and Europe, aircraft services can also be contracted from private companies and mobilized quickly for spray programs from anywhere in the world.

Table 3. Numbers of agricultural aircraft available by region (Source: Micron Group, Bromyard, UK)

Region	# of spray aircraft
North America	5,605
Central America	202
South America	3,836
Europe	89
Africa	200
Middle East	31
Central Asia	292
Far East	768
Australasia	314
Total	11,298

Geospatial Guidance Systems for Aerial Spraying

The rapid development of Global Positioning Systems (GPS) within the last 20 years has led to the uptake of this technology by almost all aircraft engaged in agricultural or public health operations. GPS systems using advanced guidance software have improved the precision of spray campaigns, and automated systems have allowed for pre-programmed flight plans, increasing the efficiency of insecticide delivery. The recent advances in spray modeling, in particular the development of Ag Disp and Ag Drift models[23,24] adapted for use in mosquito control, are now routinely used within US aerial mosquito programs to optimize delivery of spray material within the target area and minimize dose rates. These spray dispersal models can be embedded in the GPS software (e.g. Wingman GX, Adapco Inc., Sanford, FL, USA) and integrated with real time meteorological monitoring systems (e.g. AIMMS 20, Aventech Research inc., Barrie, Canada) to determine wind conditions, temperature, and humidity, providing pilots with real-time guidance. Most aircraft can also be equipped with laser altimeters to precisely record flying height, and some GPS systems allow for uploading and downloading of flight plans and treatment maps via telemetry or internet during flight so that ground monitoring teams have accurate and up to date information on the entire application process.

Non-target Organisms

In addition to carefully selecting insecticides to mitigate resistance and ensure a susceptible mosquito population, malaria programs must also consider the impact of aerial spraying on non-target organisms.[25] In a trial comparing a flat-fan nozzle system to a high-pressure nozzle system on improving the droplet spectrum of the spray in Florida, it was found that a high-pressure nozzle system substan-

tially reduced environmental contamination and led to decreased bee mortality, demonstrating the importance of application techniques. Furthermore, honey yields of hives exposed to the ULV applications did not differ significantly than those not exposed.[26,27] Similar findings were observed with space spray applications conducted in Greece.[28] Field trials in California demonstrated that low rates of application appear not to result in long-term effects if the body mass is larger than that of a mosquito. No effect of spraying was observed on non-target sentinel species including dragonflies (Sympetrum corruptum), spiders (Argiope aurantia), butterflies (Colias eurytheme), and honeybees (Apis mellifera).[29] However, monitoring for environmental contamination and non-target impacts associated with space spray applications against mosquitoes remains an area of further study.[30]

Opportunities for Malaria Elimination

Aerial application of both adulticides and larvicides for mosquito control has a long history in many parts of the world as described in this report. Given the documented success and deep experience of aerial larviciding and adulticiding for routine vector control and disease outbreak response, aerial spraying has a potential catalytic role in supporting malaria elimination efforts.

Moreover, the success of tsetse fly eradication in Africa highlights the existing infrastructure and potential transformative impact of aerial spraying on *Anopheles*. There are similarities in approaches and technologies for tseste fly control that can be leveraged for mosquito control. For example, spray dispersal techniques, GPS aircraft guidance, and spray application using rotary atomizer technology used for tsetse fly control are the same strategies used in the US and Europe for mosquito control, illustrating the readiness for aerial application in malaria elimination in Africa and elsewhere. In addition, pilots are already trained in effective insecticide application techniques that also apply to mosquitoes (i.e. application at low altitudes in early morning or late evening under favorable meteorological conditions).

Aerial spraying should be considered in the toolbox of innovative and aggressive vector control for malaria elimination. Malaria programs and their research partners can help build the evidence base, including, but not limited to, research to:

- Understand the entomological and epidemiological impact of aerial spraying on *Anopheles* populations and malaria across transmission settings and geographies;
- Examine aerial spraying in different ecological settings, e.g. rice and sugar plantations, wide flood plains, etc.
- Examine the operational feasibility and cost-efficiency of aerial spraying compared to current interventions and ground-based larviciding and adulticiding;
- Test and compare the impact and efficiency of manned versus unmanned aerial spraying on vector populations and malaria transmission; and

Evidence should inform scale-up, policy recommendations, and financing for targeted and effective use of aerial application. Guidance should also be developed on operational implementation of aerial spraying when feasible and cost-efficient, supported by robust entomological and insecticide resistance monitoring and evaluation. As ministries of health and their malaria programs continue the hard work toward elimination, aerial spraying should be considered as an important tool in the expanding vector control toolbox.

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