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RESEARCH ARTICLE

Development of a Conceptual Framework for Integrated Vector Management in the Heterogeneous Malaria Ecosystem of Western Kenya Highlands

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ABSTRACT:
Malaria heterogeneity in the highlands is due to range of factors including seasonal weather changes, climate variability, land-use changes, topography, drug resistance, and malaria control programs. High coverage of long lasting insecticide treated nets is the basis of vector control in epidemic prone western Kenya highlands. Long lasting insecticide treated nets have effectively controlled malaria in the hypo-endemic zones, but not in meso-endemic and hyper-endemic zones where significant residue of transmission remains despite control efforts.
Inadequate policy on integrated vector management application for ecologically heterogeneous ecosystems hinders effective malaria control. Advances in ecological and epidemiological studies have improved our understanding on vector distribution determinants and malaria transmission enabling us to effectively integrate indoor residual spraying into the existing long lasting insecticide treated nets programme.
Data on malaria vector abundance and parasite prevalence for different malaria ecosystems within western Kenya highlands before and after mass insecticide treated bed-net distribution campaigns was gathered to assess the efficacy of the long lasting insecticide treated nets based control efforts. Field tests were carried out to determine the impact of combined indoor residual spray and long lasting insecticide treated nets on vector indoor resting densities in zones where insecticide treated nets alone had limited efficacy or zero efficacy was observed.
Female *An. gambiae* s.l resting densities of 0.1 mosquitoes/ house/night were associated with a plasmodium falciparum (*pf*) prevalence rate of 10% or below. This observation enabled the development of a framework for the inclusion of indoor residual spray in integrated vector management with the suggestion that IRS should be applied in malaria eco-epidemiological zones where *An. gambiae* s.l resting densities exceeds 0.1 females/ house/ night.
Similarly, only those houses with a resting density of 0.1 females *An. gambiae* s.l and above should be targeted during spraying. Such an approach would significantly reduce the cost associated with indoor residual spray and provides a rationale for judicious integration of indoor residual spray within existing long lasting insecticide treated nets control programmes.

Introduction:

There exists no clear policy on integrated vector management (IVM) application in the ecologically heterogeneous ecosystems of the western Kenya highlands. Such ecosystems comprise of well and poorly drained valley systems, hills and plateaus; factors which impact vector productivity and malaria endemicity. The current national indoor residual spraying (IRS) strategy indicates blanket IRS for malaria burden reduction in endemic areas and focalized IRS in epidemic prone areas as an early response to suspected epidemics. As to exactly where IRS should be applied, the IRS strategy is unclear whether to apply in the entire affected areas or in selected hotspots. Blanket application of IRS would have been logistically and financially challenging.

In the highlands of East Africa, drivers for malaria transmission includes: climate and weather variability;[1,2] vector control;[3] anti- malarial drug sensitivity;[4] immunity;[5] and topography.[6,7] Climate variability such as that caused by El Nino southern Oscillation (ENSO) were associated with severe epidemics in the highland ecosystem.[1,8] Malaria endemicity is highly correlated to the type of drainage, hydrology and topography.[9-12] Poorly drained valley ecosystems are associated with meso-endemic to holo-endemic malaria whereas the well-drained valleys are associated with hypo-endemic malaria. Over 90% of malaria vectors are collected less than 500 meters from the valley bottoms.[13]

Prior to the 1990s there existed no vector control programs in the western Kenya highlands. Insecticide treated nets (ITNs) were implemented as part of malaria control tools following successful multi-country trials which showed significant reduction of malaria related mortality and morbidity.[14,15] In 2006, the World Health Organization endorsed scale-up in Indoor residual spraying (IRS) towards vector-borne disease.[16] World Malaria Report observes that there has been an accelerated use of IRS since 2001.[17] In Kenya, ITNs have been the tool of choice for malaria control in all ecosystems, this despite the high cost compared to IRS. The economic cost per infection case prevented by IRS was US$ 9 compared to US$ 29 for ITNs.[18]

Across Africa the current malaria interventions, though still below target levels, have substantially reduced malaria disease incidence with approximately 663 million clinical cases averted since 2000 with majority (68%) of the cases averted with ITNs.[19]

Recent advances in ecological and epidemiological studies have provided opportunities for development of a conceptual framework for IVM. Improved understanding of the ecological determinants of vector distribution and malaria transmission in western Kenya have enabled limited and targeted application of IRS for both malaria and epidemic control in the highlands. For example, since approximately 90% of indoor resting vectors were found close to the valley bottoms, application of IRS in houses within that perimeter significantly reduced malaria transmission in all houses located from the valley bottom to the top of the hill.[20]

Previously, it was assumed that IRS was most effective in reducing epidemics in the epidemic prone well drained valley ecosystem. However, following mass distribution of LLINs that reached coverage of over 80% vector abundance and infection prevalence were significantly reduced in the epidemic prone ecosystem suggesting that IRS would not have any tangible benefit in malaria epidemic control. We propose that a combined targeted and limited IRS and high ITN coverage would be more useful in areas of meso and hyper endemicity in the reduction of malaria transmission.

In this paper we present an evidence-based decision making process for identifying epidemiological situations that justify application of IRS in conjunction with the current ITN programme. Our evidence is based on previously published entomological and epidemiological data, and current data on malaria vector control interventions from studies undertaken in western Kenya highlands. The framework is based on entomological and parasitological thresholds which indicate the requirement or otherwise of concurrent application of IRS within the ITN programme.

METHODS:

Overview of concept components/ analytical framework

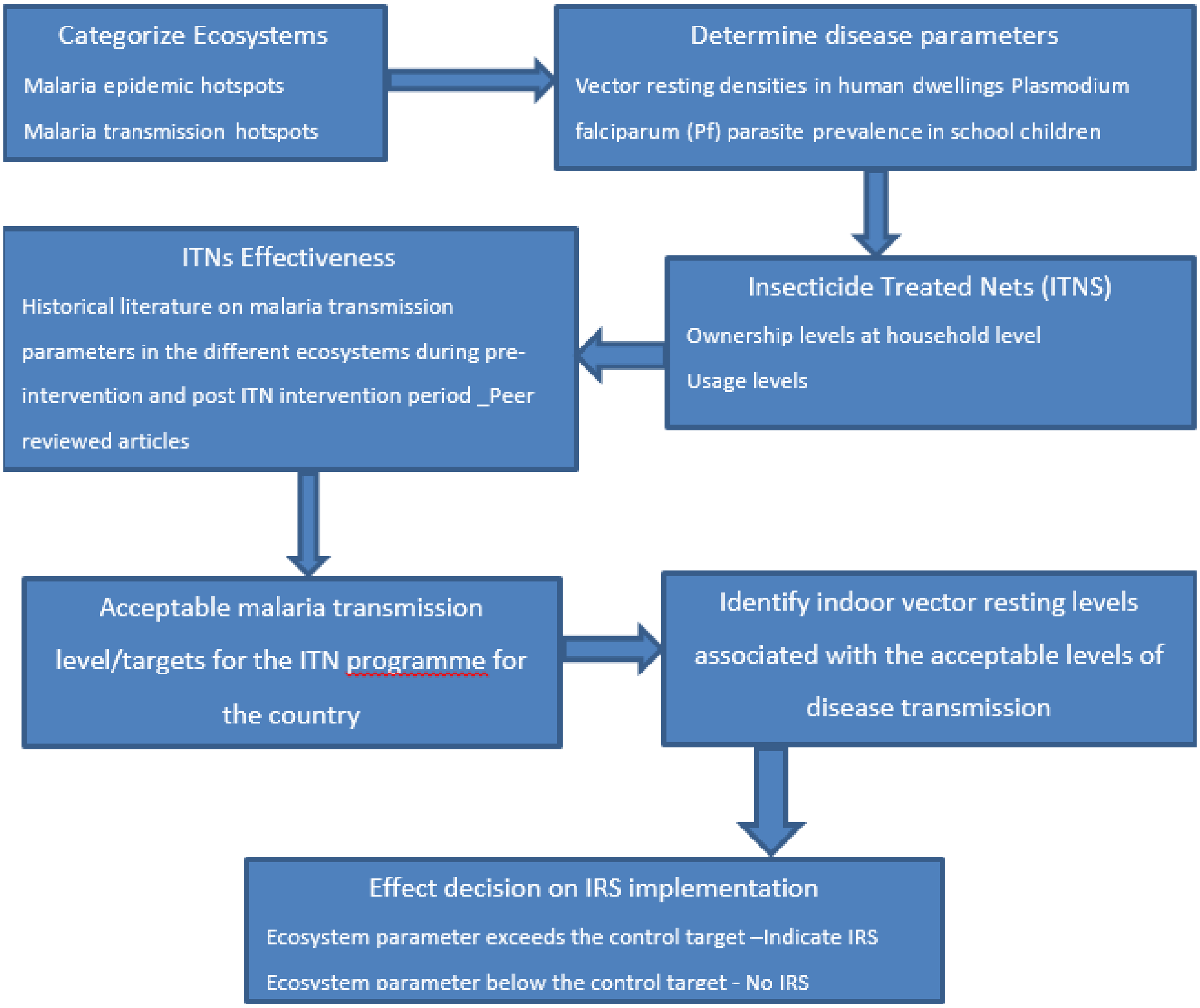

Figure 1: Overview of concept components/ analytical framework

Study sites:
Five rural villages; 3 villages i.e Iguhu {34°45'E, 00°10'N; 1430–1580 m.a.s.l} in Kakamega County; Musilongo and Emakhaha (latitude 0.0208; longitude 34.6035; altitude 1500 m.a.s.l.) both in Vihiga County representing malaria transmission hotpots and 2 villages i.e Marani (34°48'E, 00°35'S, and 1,540–1,740 m.a.s.l) in Kisii County and Fort Ternan (0°12'South and 35°20' East, 1500 to 1650 m.a.s.l) in Kericho County representing malaria epidemic hotspots) in western Kenya highlands were considered.

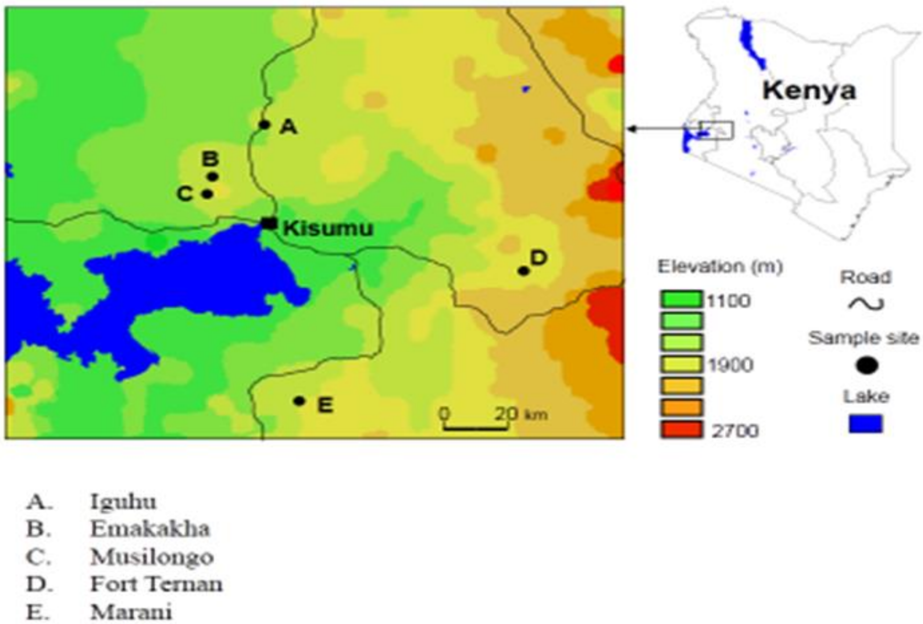

Figure 2: The map of Kenya showing the location of the 5 study sites (Courtesy, Climate and Human Health Research Unit, KEMRI)

The sites have been described elsewhere.[21,11,20,22,6,23] Site specific topographic details can be found on Google maps (https://www.google.co.ke/maps/@ 0.092234, 34.6413914, 13z? hl=en).

U (flat bottomed) and V (narrow) shaped valleys with streams and rivers, hills and plateaus define the western Kenya highland topography. Vector breeding is largely confined along the valley bottoms and approximately 95%of vectors are found less than 500 m from the breeding habitats. In flat (U shaped) bottomed valley systems, the flow of water in the streams is slow unlike in the narrow (V shaped) valley systems where water flow is fast. Poor drainage in U-shaped valley systems supports high vector densities, transmission hotspots. Good drainage in V-shaped valley systems (epidemic hotspots) supports low vector densities leading to low and unstable transmission and prone to malaria epidemics during periods of high rainfall and enormously high temperatures. At such times vector breeding occurs on sloppy hillsides causing rapid and intense transmission of malaria.[11,21,7,24]

A bimodal pattern of rainfall consisting of long rainy season from April to June and a short rainy season from October through November is experienced in western Kenya highlands. *Anopheles gambiae* Giles *sensus stricto, An. arabiensis* Patton and *An. funestus* Giles are predominant malaria vector species[13,6] and *Plasmodium falciparum* is the primary malaria parasite species.[25] *An. gambie* s.l is responsible for approximate 90% of malaria transmission hence the consideration of the vector during this study.

A review of malaria parasite (pf) prevalence, adult female An. gambiae s.l mosquito house resting densities and ITN ownership and use before and after introduction of government sponsored ITN implementation programmes

Study inclusion criteria:

Climate and human health research unit (a department within Centre for Global Health Research, KEMRI) has coordinated majority of entomological and parasitological research in western Kenya highlands since 1999 and published several papers on the same. Search engines including PubMed and Google scholar were used to access and retrieve this data.

For parasitological data, search terms: Malaria; *P. falciparum*; Prevalence; Incidence; western Kenya highlands; Kisii; Fort Ternan; Kakamega; Vihiga were included in the search. In addition to the terms used in parasitological data search: An. gambiae; An funestus; PSC; house resting densities; entomological inoculation rates; ITNs; IRS were included in the search to gather the entomological data:

Search results were restricted to articles published from the year 2000 onwards.

For parasitological data, *P. falciparum*, western Kenya highlands, prevalence and sample size, age distribution represented the outcomes of interest whereas *An. gambiae*, *An. funestus*, western Kenya highlands, indoor resting density, PSC represented the outcome of interest for the entomological data.

Identified articles were retrieved in full and checked to ascertain whether; they qualified the description provided in the inclusion criteria, and provide required information on the stated parameter.

Unpublished data from previous studies and current contemporary data qualifying the inclusion criteria were included.

In this study a 10% parasite prevalence was assumed to be an acceptable level of disease prevalence. In selecting this threshold level of parasite transmission the question of cost effectiveness of IVM should be considered and this includes determining the number of cases diverted by IVM. The fact that this level of transmission can be handled with the drugs in the existing health and vector control may not be cost effective provided the necessary justification.

Vector control intervention type and ownership determination:

Two cross sectional household surveys (pre/post mass ITN distribution campaigns in all highland districts of Kenya) were conducted for each malaria eco-epidemiological zone. In each study village a 6*4km block was identified. This was divided into 24 cells (1 km^2 each). All houses within each cell were enumerated and a distinct identification number marked on each. Similar and equal numbers were then listed on pieces of paper from among which 10-15 pieces were randomly picked to represent the specific houses to be interviewed.

Household eligibility criteria:

A household with child less than 5 years. All households that did not meet the required criteria were excluded from the study.

The first survey was conducted in August, 2010 and the second survey was conducted between January-February, 2012. A standard questionnaire was used to collect data during each survey. The questions were first written in English, translated into the local language and then back translated for clarity. The questionnaire was pre-tested in a 48 households (12 per village) after which necessary modifications and corrections were made. The questionnaire addressed: Household characteristics (demographic, socio economic status); Knowledge of malaria (transmission, symptoms, and treatment options); Control intervention (Types, implementation method, use and ownership). Interviews were conducted with the assistance of trained field staff selected from among well-disciplined and educated residents of the native community well conversed in local and cultural aspects including language. A single questionnaire was administered in each household. Respondents were identified with preference given to the household head (male or female). In case neither of the two was unavailable at the time of the interview the caretaker was interviewed. Repeat visits were made to trace the house owners in case they were unavailable during the initial visit.

Indoor resting mosquito sampling:

Site specific adult mosquito densities were determined inside randomly selected houses using pyrethrum spray collection (PSC) method.[26,27] Indoor resting adult mosquito sampling was conducted between 0630hrs and 1200hrs once every month for 20 months (May 2010-December 2011). A total of 60 houses (15 per each village: Iguhu, Musilongo, Marani and Fort Ternan respectively) were sampled each month.

Information including: date of collection, house number, eave type (open or closed), house occupants (number and gender, adults, children), mosquito control intervention tool (type, number), malaria vector (species present, sex, number and physiological status) was gathered for each individual house during each sampling visit and recorded onsite in standard field data sheets. Culicines mosquitoes were discarded while entire anopheles' mosquitoes were stored by and preserved placing them over a moist filter paper placed inside a glass Petri-dish. Separate petri-dishes containing mosquitoes collected from each house were then packed in cooler-boxes and transported to KEMRI laboratory in Kisian, Kisumu for necessary morphological identification.

IRS intervention study:

The study was informed by the outcomes of Zhou *et al.*,[28] in a densely populated uphill area in an adjacent highland site in which significant indirect impact of targeted IRS on both malaria vector and parasite density as well as the wide-reaching benefits of IRS in reducing the same for at least six months following spraying was demonstrated, suggesting targeted IRS as an effective tool in malaria control.

The field operation was carried out in Emakakha village in April 2012. A preliminary cross-sectional survey was conducted along the entire length of the Jordan valley to assess the indoor resting malaria mosquito entomological parameters (vector species composition and densities). During the survey 120 houses were randomly selected on either side of the valley. Adult mosquito sampling inside selected houses was done using Pyrethrum Spray Collection (PSC) method as described. The results clearly demonstrated that the entire valley was homogenous in terms of malaria vector parameters.

Two blocks, each measuring 2.5 km in length and separated by a 1km wide zone (buffer zone, as recommended by Zhou *et al.*,[28] were then identified on either side of the continuous homogenous valley. The two blocks were then randomly assigned the intervention and non-intervention status. In the intervention block entire walls and roofs of every human occupied house situated along either side of the valley and within a distance of 1-2km from the valley bottom were adequately sprayed with the WHO recommended dosage (25mg/m^2) of Deltamethrin 5% Wettable Powder (WP). In the non-intervention block houses were not sprayed.

Sampling of the indoor resting malaria vectors using PSC method was conducted once every month for 10 months (May – December 2012) inside 120 randomly selected houses (60 houses per each block) after intervention.

Before commencing the study, community education and mobilization activities were conducted with the involvement of all stakeholders including local administration, church leaders, village elders, teachers and community members. A field team was recruited from among recommended disciplined healthy young men and women residing in the area. The selected team was first trained on the basics of using the spray equipment's and safety gear comprising of a Standard 10litre capacity pump - Hudson® X-pert compression sprayer with HSS-8002 nozzle equipped with a regulator adjusted pressure at range 25–45 psi; Protective gear complete with fitting overalls, head gear, gumboots, and hand gloves) after which spray demonstrations were conducted. Spray equipment's and Deltamethrin insecticides (sachets) were provided courtesy of the Kenya national malaria control program. During the entire exercise a total of 1000 houses were sprayed

Rainfall data

Data on the rainfall amounts received every month in the different sites was extracted from records obtained from the Kenya Meteorological department.

Data management and analysis

Vital information on year of study, study location, study human and vector populations, indoor resting female *An. gambiae* s. l populations, malaria parasite prevalence levels, type, coverage, ownership and usage levels of control interventions were extracted from the select published and unpublished that qualified the inclusion criteria. The information was recorded and tabulated.

Pre-intervention period data utilized surveillance systems published from 2000-2005 whereas the post-intervention period data utilized surveillance systems from published 2007-2012. Annual indoor resting densities for the pre and post intervention period were averaged. *P. falciparum* prevalence associated with these indoor resting densities were determined for each ecosystem. The procedure was repeated for all other parameters including ITN ownership and usage levels.

Indoor resting mosquito data recorded in data sheets onsite during surveys were transferred into excel sheets to establish a Microsoft Excel database. Sums, monthly averages were computed directly from the Excel files.

The percentage reduction in mosquito densities for the IRS intervention study was calculated using a formula described by Mulla *et al.*,[29] to suit adult mosquito densities.

Percentage reduction=100– [C1×T2/ C2×T1] ×100

Where, C1 and C2 describe the pre and post IRS densities of resting adults in the control block and T1 and T2 in the pre and post IRS densities of resting adults in the sprayed block.

For the rainfall data primary and secondary rainfall time series were captured into MS Excel spread-sheet where seasonal rainfall totals for rainy season (short and long rains, March-May and October-December) from which annual averages were computed.

Indoor resting vector population dynamics in different seasons were obtained by plotting the monthly densities against the total amount of rainfall received each month.

Ethical considerations

Permission to conduct the study (SSC Protocol No. 1544) including scientific and ethical clearance was sought and approved by Scientific Steering Committees (SSC) and Ethics Review Committees

(ERC) of Kenya Medical Research Institute. Permission to conduct adult mosquito sampling inside selected houses and spraying houses with insecticide during the IRS intervention study was orally obtained from the heads of each household before commencement of the same.

RESULTS:

1. Literature derived historical data

Malaria parasite prevalence, An. gambiae s.l vector densities, ITN ownership and usage levels before and after mass implementation of ITN programmes

A total of 11 published studies fitting the inclusion criteria were identified as potentially relevant in this search. Majority of these studies employed the same sample size calculation based on an assumption of 50% prevalence. Similarly, 3 unpublished data sets (two from previous studies and one from the current study) were considered.

During the pre-intervention period each house within the malaria transmission hotspots had an average density of 5.0 (95% CI: 2.2-7.4) female *An. gambiae* s.l every night compared to a density of 1.0(95% CI: 0.2-1.6) female *An. gambiae* s.l per night observed in the post intervention period (Table 1). Similarly, within the malaria epidemic hotspots, houses had an average vector density of 0.3 (95% CI: 0.0-0.5) females in the pre-intervention period compared to a density of 0.2 (95% CI: 0.0-0.6) female *An. gambiae* s.l per house in the post intervention period (Table 1).

Children's from households within malaria transmission hotspots experienced an average of 57.5% malaria prevalence levels during the pre-intervention period compared to an average of 17.2% prevalence level in the post-intervention period (Table 1). In the malaria epidemic hotspots malaria prevalence levels of 10.1% were experienced among children's during the pre-intervention period compared to prevalence levels of 2.2% experienced during the post-intervention period (Table 1).

A fraction of 13.1% [95% CI: 12.8 – 13.3] households within malaria transmission hotspots owned ITNs during pre-intervention period compared to 71.8% [95% CI: 58.0- 85.0] who owned ITNs in the post intervention period. Likewise, ITN usage level of 5% [95% CI: 1.0-5.0] was observed among the households during the pre-intervention period compared to a usage level of 55.6% [95% CI: 38.0-83.0] during the post intervention period (Table 1).

In the malaria epidemic hotspots, the household ITN ownership level was 5.9% [95% CI: 0-11.8] during the pre-intervention period compared to 64.5% [95% CI: 52.3-70.0] ownership level during the post –intervention. Likewise, household ITN usage level was 7.2 [95% CI: 1.0 -14.3] during the pre-intervention period. None of the studies analysed reported ITN usage level during the post-intervention period.

TABLE 1: *An. gambiae* s.l house resting densities, malaria parasite prevalence and ITN ownership and usage levels before and after mass implementation of ITNs

Period	Year of survey	Malaria transmission hotspot: Vector resting density	Malaria transmission hotspot: Parasite prevalence	Malaria transmission hotspot: ITN ownership	Malaria transmission hotspot: ITN Usage	Malaria Epidemic hotspot: Vector resting density	Malaria Epidemic hotspot: Parasite prevalence	Malaria Epidemic hotspot: ITN ownership	Malaria Epidemic hotspot: ITN Usage	Site	Reference
Pre-Intervention	2000	7.4	68.0	-	-	-	-	-	-	Iguhu	Githeko *et al*., 2006
	2000	-	-	-	-	0.0	10.0	0.0	0.0	Fort Ternan	Koenraadt*et al*., 2004
	2000	-	-	-	-	-	10.3	-	-	Marani	Guyatt, unpublished
	2001	-	-	-	-	0.0	-	-	-	Fort Ternan	Koenraadt*et al*., 2004
	2002	2.2		-	-	-	-	-	-	Iguhu	Zhou et al., 2011
	2002	-	47.0	-	-	-	-	-	-	Iguhu	Munyekenye et al., 2005
	2002	-	-	-	-	0.5	-	-	-	Marani	Zhou et al., 2011
	2003	5.0	-	-	-	-	-	-	-	Iguhu	Ndenga et al., 2006
	2003	-	-	-	-	0.4	-	-	-	Marani	Ndenga et al., 2006
	2003	6.0	-	-	-	-	-	-	-	Iguhu	Githeko, unpublished
	2004	-	-	13.3	5.0	-	-	-	-	Iguhu	Zhou et al., 2010
	2004	-	-	12.8	-	-	-	-	-	Iguhu	Zhou et al., 2011
	2004	-	-	-	-	0.2	-	-	-	Marani	Ndenga et al., 2006
	2004	-	-	-	-	-	10.1	11.8		Marani	Zhou et al., 2011
	2004	-	-	-	-	-	-	-	14.3	Fort Ternan	Okiro et al., 2010
	2005	-	-	-	-	0.5	-	-	-	Marani	Zhou et al., 2011
Post-Intervention	2008	-	7.5	-	-	-	-	-	-	Iguhu	Zhou et al., 2011
	2008	-	-	-	-	-	1.1	65.8	-	Marani	Zhou et al., 2011
	2009	1.1	16.9	72.0	62.3	-	-	-	-	Iguhu	Atieli et al., 2011
	2009	1.6	9.0	70.0	49.2	-	-	-	-	Musilongo	Atieli et al., 2011
	2009	-	13.0	-	-	-	-	-	-	Iguhu	Zhou et al., 2011
	2009	-	-	-	-	0.5	-	-	-	Marani	Ototo et al., 2011
	2009	-	-	-	-	0.5	-	-	-	Fort Ternan	Ototo et al., 2011
	2009	-	-	-	-	-	-	70.0	-	Marani	Githeko, unpublished
	2009	-	-	-	-	-	-	70.0	-	Fort Ternan	Githeko, unpublished
	2010	1.4	-	-	-	-	-	-	-	Iguhu	Current, unpublished
	2010	0.8	-	-	-	-	-	-	-	Musilongo	Ototo et al., 2011
	2010	0.2	-	-	-	-	-	-	-	Musilongo	Current, unpublished
	2010	-	16.9	60.3	51.0	-	-	-	-	Iguhu	Zhou et al., 2011
	2010	-	12.6	-	-	-	-	-	-	Iguhu	Ototo et al., 2011
	2010	-	23.3	-	-	-	-	-	-	Iguhu	Wanjala et al., 2011
	2010	-	21.9	-	-	-	-	-	-	Musilongo	Wanjala et al., 2011
	2010	-	-	58.0	38.0	-	-	-	-	Musilongo	Zhou et al., 2011
	2010	-	-	-	50.0	-	-	-	-	Iguhu	WHO report 2011
	2010	-	-	-	-	0.6	2.8	-	-	Marani	Ototo et al., 2011
	2010	-	-	-	-	0.0	-	-	-	Marani	Current, unpublished
	2010	-	-	-	-	0.0	-	-	-	Fort Ternan	Current, unpublished
	2010	-	-	-	-	-	2.0	52.3	-	Marani	Zhou et al., 2011
	2010	-	-	-	-	-	2.9	-	-	Fort Ternan	Wanjala et al., 2011
	2010	-	-	-	-	-	2.4	-	-	Marani	Wanjala et al., 2011
	2011	0.3	-	-	-	-	-	-	-	Iguhu	Current, unpublished
	2011	1.0	-	-	-	-	-	-	-	Musilongo	Atieli et al., 2011
	2011	0.4	-	-	-	-	-	-	-	Musilongo	Current, unpublished
	2011	-	-	78.3	-	-	-	-	-	Iguhu	Zhou et al., 2013
	2011	-	-	85.0	83.0	-	-	-	-	Musilongo	Zhou et al., 2011
	2011	-	-	74.0	-	-	-	-	-	Iguhu	Atieli et al., 2011
	2011	-	-	76.7	-	-	-	-	-	Iguhu	Zhou et al., 2014
	2011	-	-	-	-	0.2	-	-	-	Marani	Current, unpublished
	2011	-	-	-	-	0.1	-	-	-	Fort Ternan	Current, unpublished

2. Contemporary data

Vector control intervention types, ownership and usage levels:

A total of 1000 household were interviewed during the two surveys. IRS and insecticide treated nets (ITNs) comprised the main vector control interventions in both malaria transmission and epidemic hotspots.

Table 2: Availability, ownership and usage levels of the main malaria vector control interventions, in different malaria transmission zones before and after 2011 mass distribution of ITNs.

Survey period	Type of malaria ecosystem	Sample households (n)	Houses with IRS	Houses with ITNs	Total ITNs owned	Average. ITNs per house	ITNs in use	Av. ITN in use
2010	Transmission	302	120 [39.7]	214 [70.9]	388	1.3	332	1.1
	Epidemic	301	9 [3]	176 [58.5]	318	1.1	282	0.9
2011	Transmission	200	77 [38.5]	183 [91.5]	469	2.4	346	1.7
	Epidemic	200	151 [75.5]	187 [93.5]	463	2.3	406	2.0

*Figures in parenthesis represent percentages

Prior to the mass distribution of ITN 70.9 % of the households within the malaria transmission hotspots owned at least one ITN compared to 91.5% households that owned ITNs after the mass distribution (Table 2). The average number of ITNs owned in each house before the mass distribution was 1.3 nets compared to an average of 2.4 nets owned after the mass distribution (Table 2). An average 1.1 bed nets were regular use each night before the mass distribution campaign compared to an average 1.7 ITNs used regularly every night after the mass distribution campaign (Table 2). In the malaria epidemic hotspots 58.5% households owned at least one ITN prior to the distribution compared to 93.1% households that owned at least one ITN after the mass distribution in 2011. Each household owned an average of 1.1 net before the mass distribution compared to 2.3 nets owned by each household after the mass distribution. An average of 0.9 ITNs were actually used each night per each household before the mass distribution campaign compared to 2.0 ITNs used per household every night after mass distribution campaign (Table 2). Within the malaria transmission hotspots 39.7% of the households had their walls sprayed before the mass ITN distribution campaign compared to 38.5% sprayed households after the mass distribution campaign (Table 2). Within the malaria epidemic hotspots only 3% of the households had IRS before the mass ITN distribution campaign compared to 75.5% households with IRS after the mass campaign (Table 2).

Indoor resting density and anopheles vector species composition:

A total of 295 adult female anopheles mosquitoes, comprising 284 [96.7%] *An. gambiae* s.l and 11 [3.7%] *An. funestus* mosquitoes were collected during the study. Of the 11 adult female *An. funestus* mosquitoes, 7 [63.6%] were collected from the epidemic hotspots while 4 [36.3%] were collected from transmission hotspots

Of the 284 adult female *An. gambiae* s.l mosquitoes 243 [85.6%] were collected in malaria transmission hotspots while 41 [14.4%] were collected from the malaria epidemic sites.

Table 3: Average densities of female *An. gambiae* s.l mosquitoes resting inside houses in different malaria eco-epidemiological sites

		Transmission hot spots		Epidemic hot spots	
Year	Month	Iguhu	Musilongo	Marani	Fort Ternan
2010	May	4.7	0.2	0.1	0.0
	Jun	4.8	0.4	0.0	0.0
	Jul	1.2	0.4	0.0	0.0
	Aug	0.2	0.1	0.0	0.0
	Sep	0.3	0.1	0.0	0.0
	Oct	0.0	0.0	0.0	0.0
	Nov	0.1	0.4	0.0	0.0
	Dec	0.2	0.3	0.2	0.0
2011	Jan	0.0	0.2	0.0	0.0
	Feb	0.5	0.2	0.1	0.0
	Mar	0.4	0.4	0.0	0.0
	Apr	0.0	0.8	0.0	0.0
	May	0.0	0.7	0.3	0.0
	Jun	1.3	0.9	0.7	0.0
	Jul	0.3	0.2	0.2	0.0
	Aug	0.0	0.2	0.0	0.0
	Sept	0.8	0.5	0.5	0.2
	Oct	0.3	0.7	0.5	0.4
	Nov	0.1	0.6	0.1	0.1
	Dec	1.2	0.6	0.7	0.0

Overall, the average indoor resting density was 0.5females/house/night in the malaria transmission hotspots compared to 0.1 females/ house/night in malaria epidemic hotspot (Table 3).
Highest vector densities in both the malaria transmission and epidemic hotspots were observed in the month of June (Figure 3). The observed trend does not clearly depict a direct relationship between the vector resting densities and the amount of rainfall received during the month.

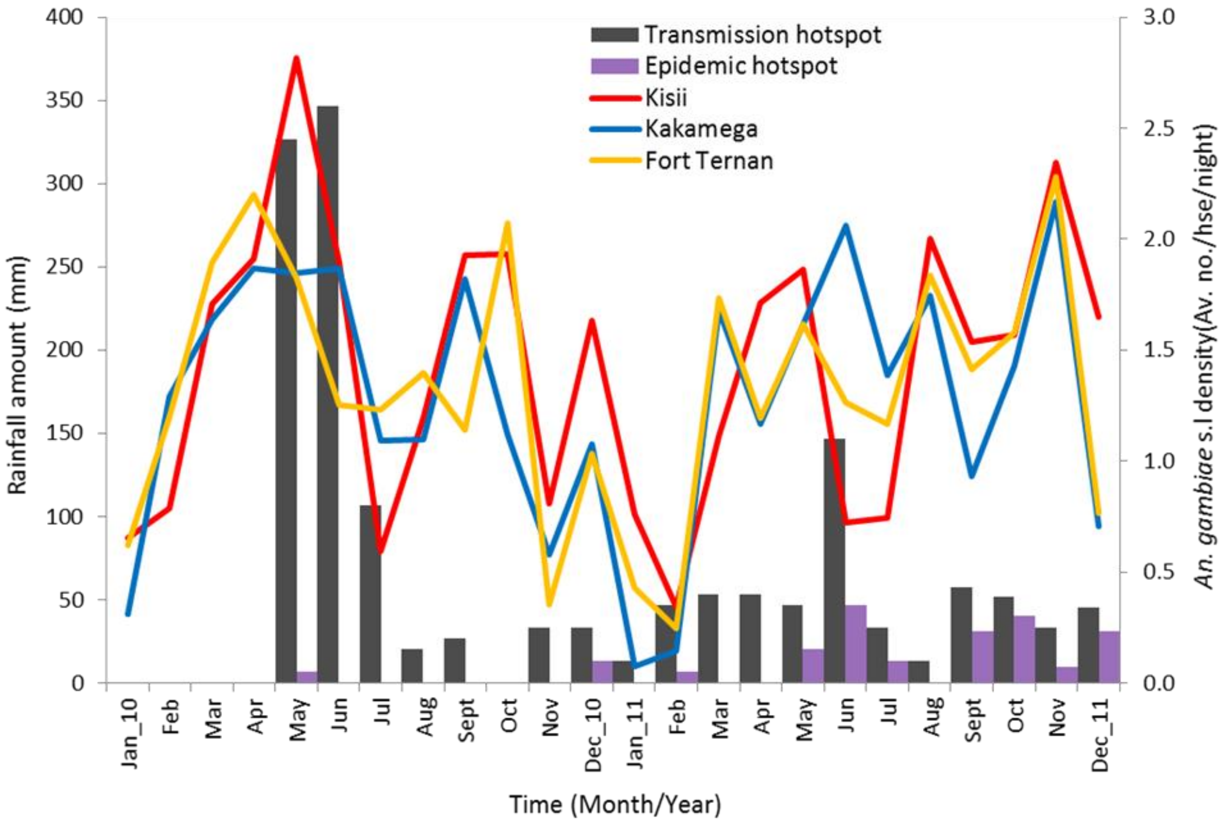

Figure 3: Amount of rainfall received and density of indoor resting adult female *An. gambiae* s.l in different malaria eco-epidemiological zones.

Indoor resting vector abundance in the IRS intervention and non-intervention sites:

Houses within the intervention and non-intervention block were similar in respect to the vector resting densities prior to the commencement of the intervention study.

Table 4: Female *An. gambiae* s.l mosquito densities within IRS sprayed and non-sprayed houses

Time (months)	Time lapse prior or post intervention (months)	*An. gambiae*s.l density in non-intervention site (average no. per house/night)	*An. gambiae*s.l density in intervention site (average no. per house/night)	% reduction in *An. gambiae*s.l densities
March	-1	0.9	0.9	0
April	0	-	-	-
May	1	0.5	0.1	80.0
June	2	0.7	0.0	100.0
July	3	0.2	0.1	50.0
August	4	0.2	0.1	50.0
September	5	0.6	0.2	66.7
October	6	0.3	0.5	-66.7
November	7	0.4	0.2	50.0
December	8	0.5	0.2	60.0

One month after spraying IRS resulted in 80% reduction in average adult *An. gambiae* s.l mosquito densities resting inside each sprayed houses from 0.5 to 0.1 (females/house/night). In the second month a 100% drop in *An. gambiae* s.l densities was observed in the sprayed houses. An average density of 0.7 female *An. gambiae* s.l/house/night was recorded in the non-intervention site compared to zero females/house/night recorded in the intervention block compared to (Table 4). Reductions in *An. gambiae* s.l densities were observed in the first 4 months after spraying after which the densities increased (Table 4).

DISCUSSION:

Due to climate change and land use changes malaria prevalence has spread to western and central Kenya highlands as well as elsewhere in east and central Africa.[30,31] There was an urgent need to formulate the vector control strategies with the aim of preventing epidemics and controlling endemic malaria transmission in these highlands.

Historically IRS was effectively used to control malaria in different areas including; Rhodesia (current Zimbabwe), Swaziland and Zanzibar.[32]

It is notable that IRS was most effective in areas that have a single transmission season or areas with very low transmission. In areas of intense transmission IRS is not able to provide a year round protection due to its short period of persistence on sprayed surfaces. In some cases, a least two rounds of spraying would be required. In addition, whereas the long lasting ITNs can control the vectors for 3-5 years IRS requires repeated annual applications making the method unrealistic and financially challenging.

Our study examines whether IRS has a role in the control of endemic malaria in the highlands of western Kenya. Early trials suggested that IRS could be used in areas that were prone to malaria epidemics.[18] However, at that time malaria epidemics were unpredictable thus nullifying the use of IRS as a preventative tool.

Following the large scale trial of ITNs across Africa it was shown that a significant impact of reduction in all-cause mortality was attributable to this form of malaria intervention.[15,14] Introduction of LLINs improved the efficacy of this intervention tool due to the decreased need for a net re-impregnation with insecticide. The LLINs technology was adapted as a primary tool for vector control in malaria endemic zone in Africa and elsewhere. The application of IRS in an environment of wide scale LLINs has not been well understood.

The highlands are complex ecosystems comprising of hills, valleys and plateaus. The drainage system varies from slow flowing rivers and streams to fast flowing streams.[24,33] These ecological systems form distinct malaria eco-epidemiological stratifications with some areas having high perennial transmission while others have epidemic prone transmission.[11] Epidemiological studies across these distinct ecosystems have indicated that mass application of LLINs have significantly reduced malaria transmission in epidemic prone areas to about 1–2%.[20] However, whereas a significant reduction in transmission has been achieved in the transmission hotspots (consider c.a 60%, Githeko *et al.*,[12] prevalence during pre-intervention period vs. 17.2% post-intervention period), there is still need for a further reduction in transmission so as to minimize the public health risk of malaria.

Currently there exists no framework for the concurrent use of IRS and LLINs. In order to develop such a framework, we reviewed existing entomological and parasitological data obtained the period before and after the wide scale application of LLINs. Whereas the pre-intervention data included the period 2000-2005, post-intervention data covered the period 2006-2011. From the review data it was shown that in the epidemic-prone zone the wide scale use of LLINs reduced the problem of malaria from an average of 10% to 2.0%. In the transmission hotspot the prevalence declined from an average of 57% to 17%. The concurrent vector density data indicated a decrease from an average density of 5.0 to 1.0 female *An. gambiae* s.l mosquitoes per house per night. In the epidemic transmission zones, the changes in vector density before and after the intervention period were less clear. Density remained the same for both pre and post intervention at an average density of 0.2 Females/house/night. It is however known that in the post-intervention period no vectors were detected in houses in epidemic zone for several months[21] but in pre-intervention period vectors were breeding throughout the year.[34] A key component of the framework for the application of IRS in these ecosystems is the determination of a critical threshold of indoor resting densities in order for the intervention to be associated with an acceptable public health level of malaria prevalence. It should be noted that vector control method in whatever form (single intervention or integrated vector management) should ideally eliminate transmission. However, to achieve this ideal is a significant challenge. Based on the available published data an average density of 0.2 Females/house/night was associated with average malaria prevalence of 10% and below. Therefore, we propose that any vector control programme should aim at obtaining a mean annual vector density of 0.2 female *An. gambiae* s.l /house/night and below. Arising from this proposition it is clear that LLINs distribution of greater than 80% is associated with malaria prevalence of 10% and below. In fact, the average prevalence of malaria following the wide scale implementation of LLINs in epidemic-prone hotspots was 2.0%. Thus, it may not be critically important to introduce IRS given the low malaria prevalence in this ecosystem. On the other hand, LLINs ownership levels above 80% in the transmission hotspots did not achieve the critical threshold of malaria prevalence i.e. 10% and below. In addition, the vector density remained well above the framework threshold of an average 0.2 *An. gambiae* s.l females/house/night. It is therefore proposed that an integrated vector management scheme should be adopted in these ecosystems and this should include a concurrent system of targeted IRS. This concept was tested by applying IRS in houses along the valley bottom and adjacent to the major breeding habitats Emakhaha village, Vihiga County, western Kenya. The application of IRS resulted to a reduction in the resting densities from an average of 0.7 to 0.0 *An. gambiae* s.l mosquitoes per house during the second month after application. The acceptable suppression of less than 0.2 females per house was observed for four months in a transformation season. An earlier similar study in an adjacent site observed similar outcomes.[28] IRS may be used in the epidemic hotspots to prevent epidemics if epidemic risk is detected using currently available models e.g. meteorological driven epidemic early warning systems.[35]

Our monthly indoor vector surveillance density data indicates high vector densities from May-July 2010 followed by a period of relatively low densities. IRS should be used to suppress high vector densities during the long rains (April-May-June). Overall our data indicates that the amount of rainfall received had limited impact on the observed vector densities contrary to the observation of an earlier study.[6]

Increased effort by the government to provide free LLINs through mass distribution campaigns in entire highland sites, last such campaign having been conducted between May and August 2011 could largely explain the observed difference in bed net ownership and usage between the two surveys. It should be noted that during such distribution campaigns a lot of community mobilization and awareness activities on the benefits associated with LLINs is done. A major challenge though to the effective implementation of ITNs is usage as observed during the surveys that net ownership does not guarantee full utilization and use.

Arising from the foregoing analysis a conceptual framework for the implementation of appropriate malaria control interventions in western Kenya highlands was constructed based on the observed indoor resting densities and associated parasite. This conceptual framework provides a guide to evidence based IVM.

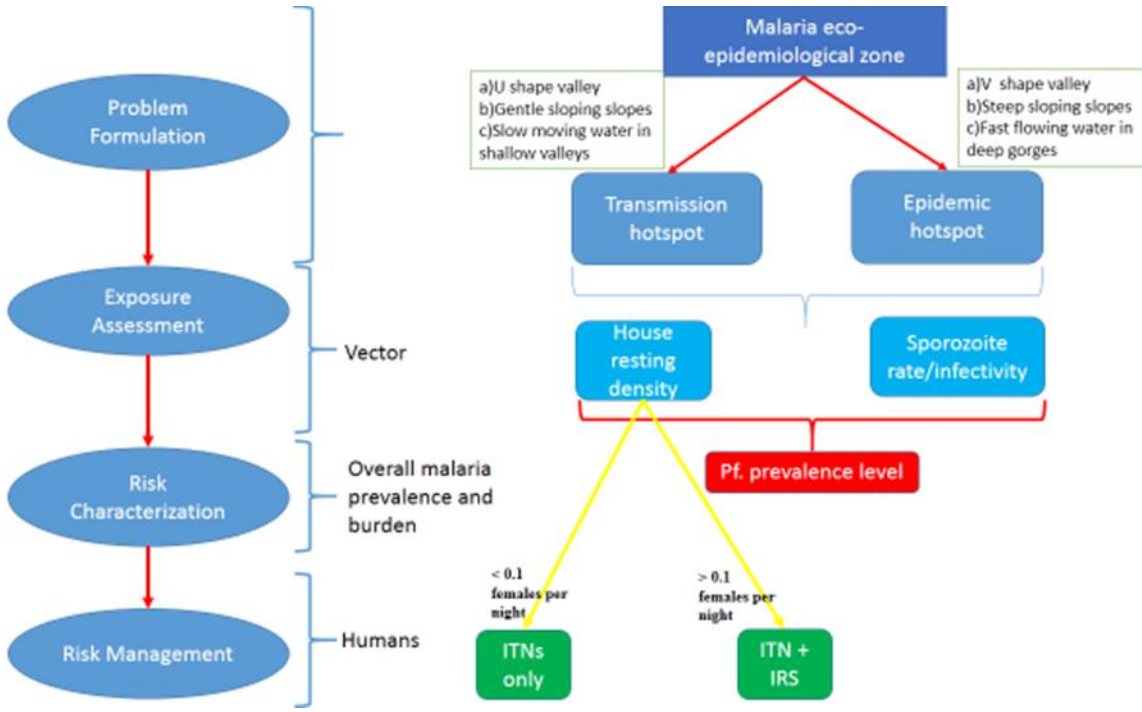

Figure 4: A rational decision making framework for the implementation of appropriate malaria control interventions in western Kenya highlands.

Conclusion:
Malaria epidemic hotspots are defined with ecosystems with good drainage whereas the transmission hot spots are defined by ecosystems with poor drainage and high malaria transmission. Proper understanding of the different eco-epidemiological zones could yield the relevant knowledge that will create an important and stable foundation of improving the existing interventions and designing new and more effective ones.

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