RBM Partnership
To End Malaria

7 February 2023

Expanded Vector Control Toolbox in Humanitarian Settings

Talk 3:
Phase III study on Durable Wall Lining in Liberia

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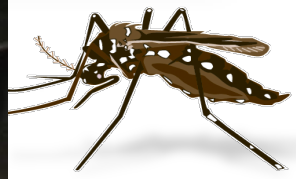
Durable Wall Lining

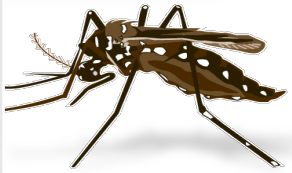
Dual purpose (2 generations) designed to:

- Protect displaced communities returning to their homes, and stable communities alike
- Provide aesthetic home improvement that is desired by rural households
- Be installed onto the surface of inner walls, of rural houses
- Screen eve gaps, windows, ceilings
- Kill resting mosquitoes (mode of action = IRS)
- Significantly reduce malaria
- Provide consistent delivery and dosage of insecticide over multiple years

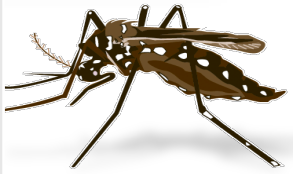


DL Prior Published Evidence

	Country	Year	Author	Journal	Title
1	*Laboratory*	2011	Achee NL, et al.	61st ASTMH meeting	Evaluation of ZeroVector® Durable Lining (DL) – impact on *Aedes aegypti* and *Anopheles stephensi* under varying DL coverage
2	Kenya	2011	Gimnig J	61st ASTMH meeting	Insecticide-treated wall liners reduce malaria transmission in Kenya
3	Papua New Guinea	2012	Pulford J, et al.	Malaria Journal	Feasibility and acceptability of DL for vector control in Papua New Guinea
4	Angola	2012	Brosseau L, et al.	PLoS One	Human antibody response to *Anopheles* saliva for comparing the efficacy of three malaria vector control methods in Balombo, Angola
5	Angola, Nigeria	2012	Messenger L, et al.	Malaria Journal	The development of insecticide-treated durable wall lining for malaria control: insights from rural and urban populations in Angola and Nigeria
6	Equatorial Guinea, Ghana, Mali, South Africa, Vietnam	2012	Messenger L, et al.	Malaria Journal	Multicentre studies of insecticide-treated durable wall lining in Africa and South-East Asia: entomological efficacy and household acceptability during one year of field use



	Country	Year	Author	Journal	Title
7	Tanzania	2016	Mtove G, et al	BMC Public Health	The effectiveness of non-pyrethroid insecticide-treated durable wall lining to control malaria in rural Tanzania: study protocol for a two-armed cluster randomized trial
8	India	2016	Mondal D, et al	PLOS NTD	Efficacy, Safety and Cost of Insecticide Treated Wall Lining, Insecticide Treated Bed Nets and Indoor Wall Wash with Lime for Visceral Leishmaniasis Vector Control in the Indian Sub-continent: A Multi-country Cluster Randomized Controlled Trial
9	Tanzania	2017	Kweka E, et al	BMC Res Notes	Bio-efficacy of deltamethrin based durable wall lining against wild populations of *Anopheles gambiae* s.l. in Northern Tanzania
10	Global	2017	Messenger L, et al	Malaria Journal	Insecticide-treated durable wall lining (ITWL): future prospects for control of malaria and other vector-borne diseases
11	Tanzania	2017	Emidi B, et al	BMC Res Notes	Impact of non-pyrethroid insecticide treated durable wall lining on age structure of malaria vectors in Muheza, Tanzania
12	Tanzania	2021	Mpangala K, et al	BMC Public Health	On the cost-effectiveness of insecticide-treated wall liner and indoor residual spraying as additions to insecticide treated bed nets to prevent malaria: findings from cluster randomized trials in Tanzania.



Durable wall lining for malaria control in Liberia: results of a cluster randomized trial

Aim: To determine the malaria control efficacy of DWL.

Primary Objective: To determine if DWL has an additional protective effect in an area of pyrethroid resistance.

Secondary Objectives: To compare surface bio-availability of insecticides and entomological effectiveness over the study duration.

Freetown
Sierra Leone
Koidu
Macenta
Tokbombu
Bo
Kenema
Sopota
Nzerekore
Man
Ganta
A8
Gbarnga
Duekc
A701
Monrovia
Liberia
Zwedru
A7
Helomeh
Harper
Google

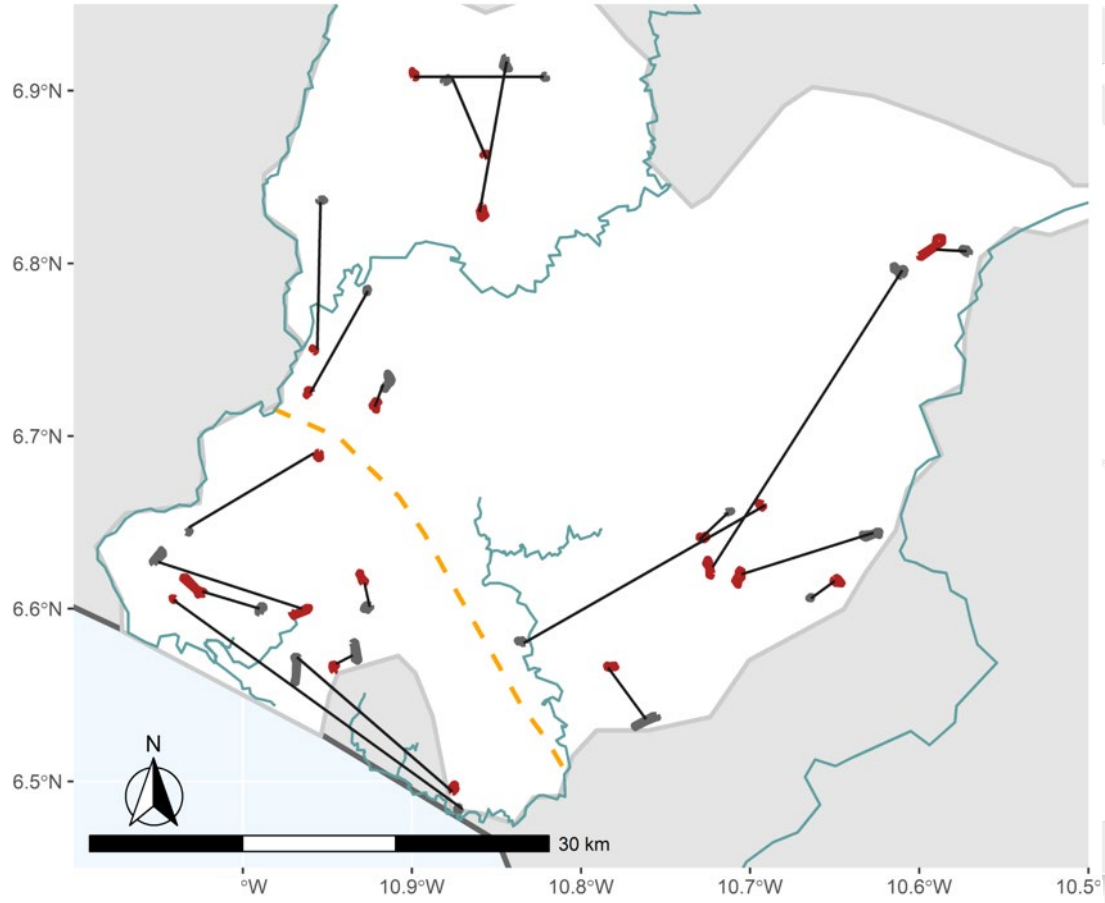
Cluster Randomized Trial Design

Participants: 2 - 59 months

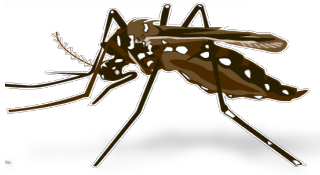
Cluster villages randomly allocated to control or active arms, and paired on 4 covariates: *P. falciparum* prevalence, population size, LLIN usage & district.

Control Arm: 50 houses per 20 clusters, all of which received LLIN within the previous 12 mts

Bomi County (Upland and Coastal Divisions)

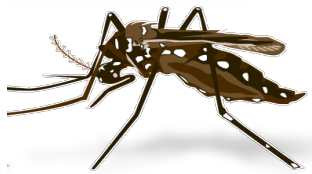


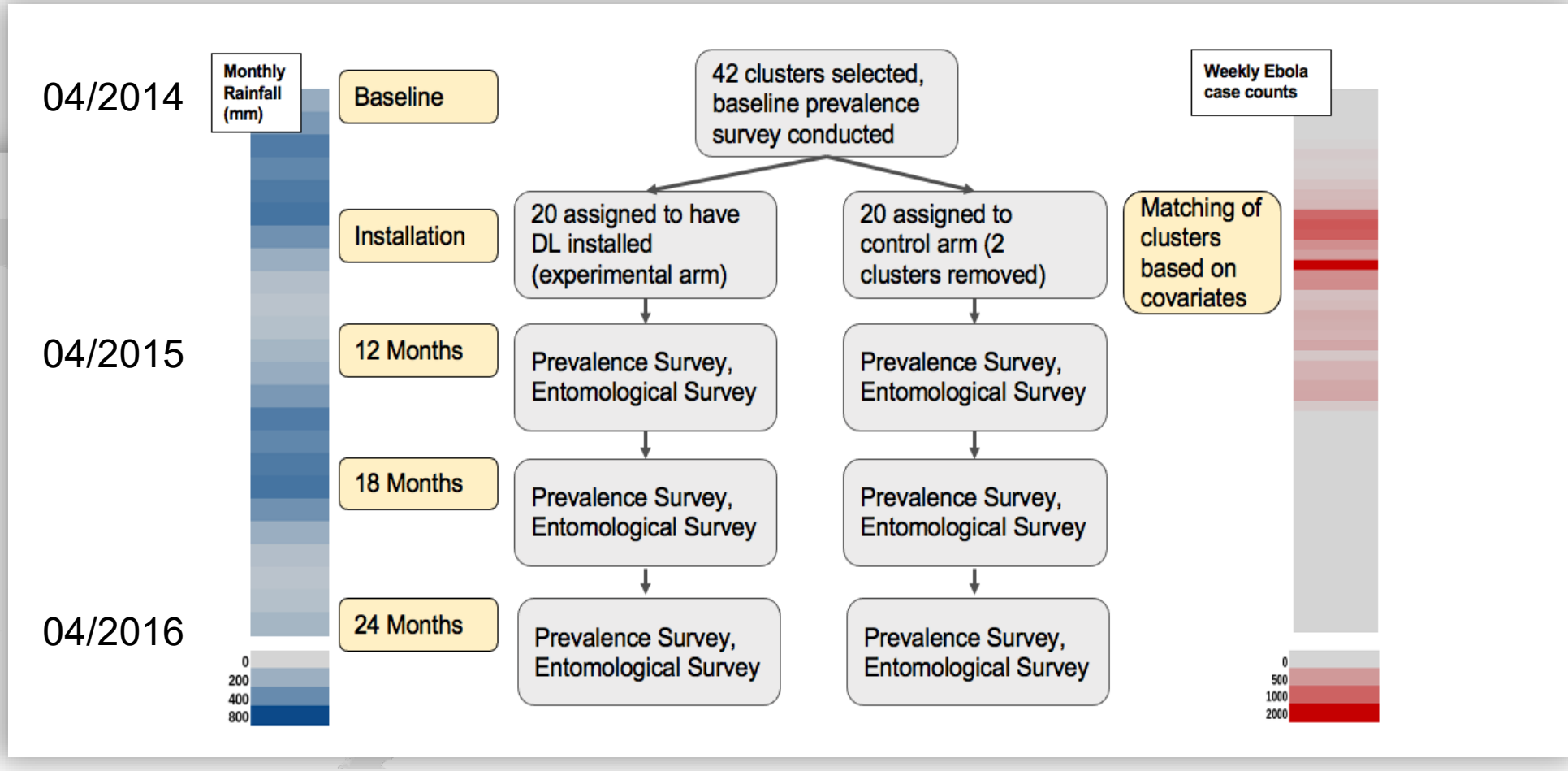
Active Arm: 50 houses per 20 experimental clusters, all of which received LLINs with the previous 12 mts, and had internal walls and ceilings lined with DWL.



Housing Design in Trial Sites

- DWL: Vestergaard
- Non-woven polypropylene
- Fenpyroximate and abamectin
- Fenpyroximate is a NADH-coenzyme Q reductase inhibitor (IRAC 21a)
- Abamectin acts on the glutamate-gated chloride channel (IRAC 6).
- Neither used in mosquito control previously
- The non-woven material had no additional surface treatments.





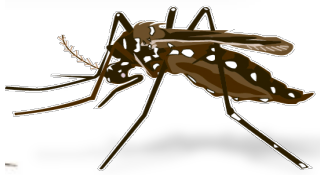
- Participants recruited in 42 clusters for baseline epi. survey.
- Surveys conducted every 6 months, with the exception of 6 months after baseline due to Ebola virus disease restrictions.
- Weekly Ebola case counts are shown as a red colour gradient.
- Rainfall amounts (seasons) shown as a colour gradient in blue.

Epidemiological Outcome Measures

- At baseline, an epidemiological survey of all children 2 months to 59 months of age was conducted in 40 clusters.
- Age, sex, tympanic temperature were recorded and children were tested for P. falciparum infection with SD Bioline Pf RDT.
- All RDT positive cases were treated with artesunate amodiaquine.
- The epidemiological survey was repeated after DWL installation at 12, 18 and 24 months.
- All children were recruited regardless of whether they participated in earlier surveys.

Surveys at 12, 18 and 24 months following baseline were conducted during Ebola virus transmission and were subject to increased infection control protocols.

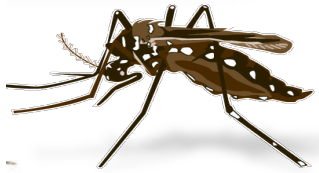
This meant that febrile (by infrared thermometer) or other symptomatic children were excluded from the study. Between monitoring periods the NGO continued to support healthcare throughout the region.

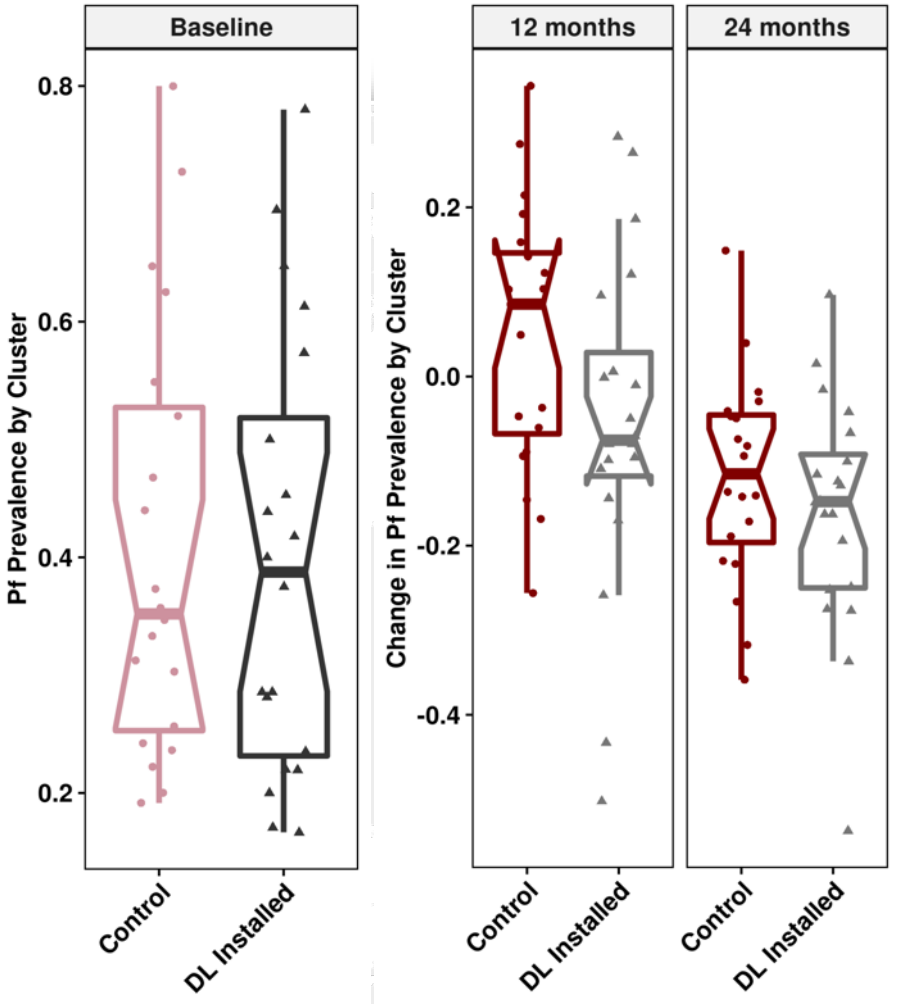


Entomological Effectiveness Outcome

- Baseline resistance profile in wild-caught mosquitoes conducted (WHO guidelines).
- Bioefficacy (12 & 24 months) against An. gambiae s.l. mosquitoes was determined by collecting larvae from three sites in Bomi County.
- Larvae were reared to adults and females were tested in WHO cone bioassays modified from WHOPES LLIN guidelines.
- DWL samples (30 × 30 cm) from consenting households were taken at 2 m above the floor and the resulting holes were patched.
- Female mosquitoes aged 2–5 days post eclosion were exposed at a 45° angle for 30 min with 10 mosquitoes per cone and placed in holding cups for 72 h.

Due to the variability in assay conditions and wild-caught mosquitoes, the allowable control mortality at 72 h was extended to 20%. Mean mortality was calculated for 12 samples collected at time of installation and 129 samples collected 12 months post installation.





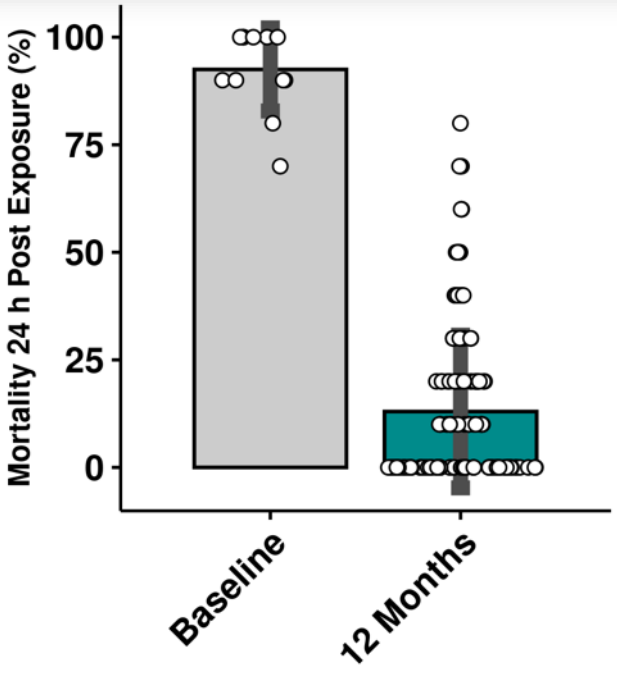
Baseline balance in Pf prevalence between study arms.

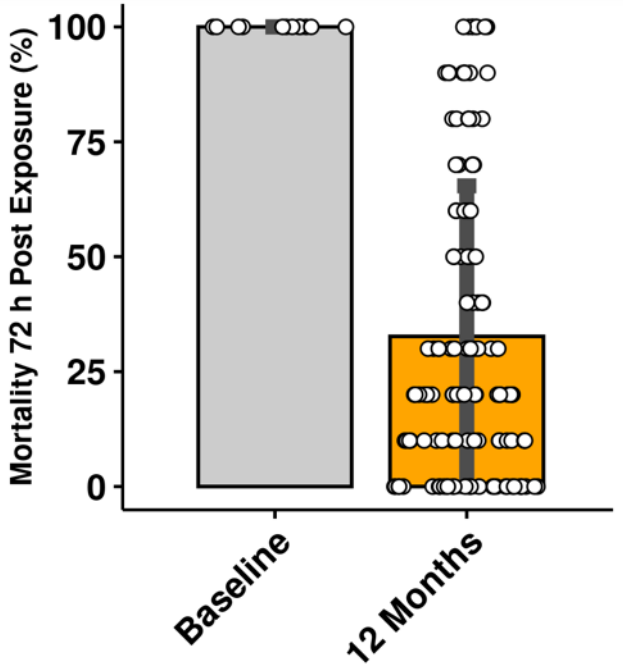
Change in proportion of Pf prevalence from

- Baseline to 12 months &
- From baseline to 24 months

Boxplot represents mean, interquartile range, whiskers represent range, notch represents 95% confidence interval.

WHO Cone Bioassays





Mortality of An. gambiae s.l. following exposure to fenpyroximate abamectin treated DWL, observed at 24 and 72 h post exposure in WHO cone bioassays.

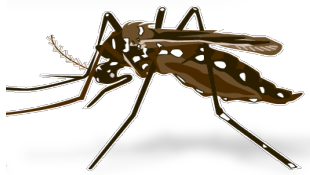
Bars = mean of replicates, dots = individual bioassays, error bars = standard deviation.

Epidemiological effect of DWL in 20 paired clusters Bomi County, Liberia.

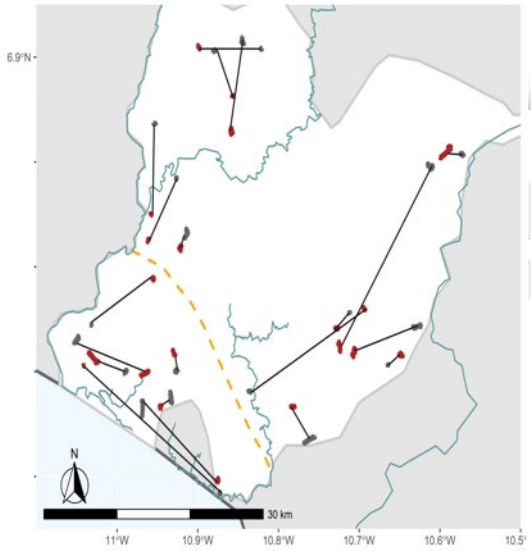
Paired clusters with their corresponding village names and cluster numbers are shown along with whether they were randomized to receive DWL or not.

Village Name	Pair Number	DL Installed	Region	Pf Prevalence Apr 2014 (Baseline)	Pf Prevalence Apr 2015	CMH Pooled RR	Pf Prevalence Nov 2015	CMH Pooled RR	Pf Prevalence Apr 2016	CMH Pooled RR
Big Geveh	1	No	Upland	0.468	0.431	RR=1.30 P=0.022	0.303	RR=0.85 P=0.215	0.427	RR=1.26 P=0.133
Madina Levekai		Yes		0.418	0.538		0.565		0.302	
Junk-Sonodee	2	No		0.800	0.632		0.457		0.629	
Suehn		Yes		0.780	0.278		0.214		0.243	
Boakai	3	No		0.200	0.304		0.216		0.106	
Kpakla		Yes		0.400	0.320		0.417		0.206	
Zuwah	4	No		0.357	0.571		0.370		0.275	
Sumo		Yes		0.500	0.241		0.404		0.225	
Nyandehun Gwenpolu	5	No		0.242	0.292		0.517		0.391	
Nyalowahun		Yes		0.286	0.206		0.613		0.185	
Gbai	6	No		0.727	0.633		0.519		0.767	
Small Geveh Kanela		Yes		0.613	0.517		0.386		0.450	
Folley	7	No		0.625	0.536		0.639		0.308	
Gbojay		Yes		0.647	0.214		0.491		0.310	
Ngardor	8	No		0.333	0.273		0.724		0.259	
Kissi		Yes		0.453	0.283		0.675		0.204	
Besao	9	No		0.373	0.565		0.500		0.155	
Damah		Yes		0.286	0.292		0.438		0.244	
Zarmeyan	10	No		0.520	0.606		0.214		0.471	
Zui		Yes		0.695	0.551		0.545		0.418	
Budding	11	No		0.647	0.750		0.370		0.600	
Dependent		Yes		0.574	0.475		0.694		0.321	
Bola	13	No		0.549	0.634		0.308		0.190	
Beajah		Yes		0.439	0.722		0.485		0.276	
Zalakai	14	No		0.440	0.563		0.385		0.174	
Barmore		Yes		0.281	0.280		0.379		0.296	
Bugbay	15	No		0.222	0.381		0.125		0.080	
Dean		Yes		0.167	0.353		0.462		0.263	
Kpagbula	16	No	Coastal	0.191	0.333	RR=1.30 P=0.344	0.125	RR=0.94 P=0.665	0.162	RR=1.13 P=0.529
Vortor-Tombekai-Karnikorn		Yes		0.220	0.170		0.321		0.073	
Weajor	17	No		0.313	0.167		0.459		0.091	
Gbanga-Kpah		Yes		0.235	0.500		0.355		0.111	
Gomai Krusaw	18	No		0.236	0.189		0.262		0.100	
Dagweh		Yes		0.171	0.100		0.265		0.042	
Kalagban Bonah	19	No		0.303	0.578		0.558		0.162	
Bogbeh		Yes		0.375	0.471		0.565		0.226	
Saah Charlie	20	No		0.256	0.600		0.417		0.238	
Wolokai		Yes		0.200	0.091		0.205		0.133	
Nyama-Farnila	21	No		0.347	0.091		0.442		0.158	
Menkor-Peeyan		Yes		0.220	0.209		0.547		0.204	
			N	1706	1305		1624		1682	

Bioefficacy of Abamectin+Fenpyroximate	93%	13%



Results



- Installation of DWL resulted in a significant reduction of P. falciparum malaria prevalence 12 months later in the 28 Upland clusters of the study (RR = 1.3, p=0.022).
- This effect was not seen in the 12 Coastal clusters at 12 months (RR = 1.3, p=0.344).
- A difference between study arms was not observed at 18 or 24 months following the baseline survey.
- This reduction in control effect coincided with a significant reduction in bioavailability of insecticides on the DWL after 12 months.

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Conclusions

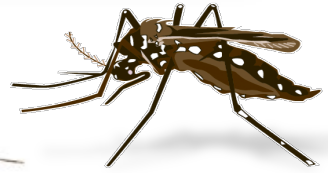
DWL is feasible to install and easy maintain with high levels of acceptance, even in an Ebola epidemic.

A highly adaptable tool that can be installed into a wide range of structures.

Designed for returnees, but applicable for most communities / structures in stable settings.

It significantly helps to prevent malaria infections in inland high transmission settings (uplands).

It may provide multi-year protection with further chemical/materials development



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Acknowledgements & Further Reading

Colleagues in PMI who contributed to the trial protocol design.

Colleagues who worked with me to help deliver this study:

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Durable wall lining for malaria control in Liberia: results of a cluster randomized trial. Malar J 22, 15 (2023). https://doi.org/10.1186/s12936-022-04429-7

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