



Advancing Evidence for
the Global Implementation of
SPATIAL REPELLENTS

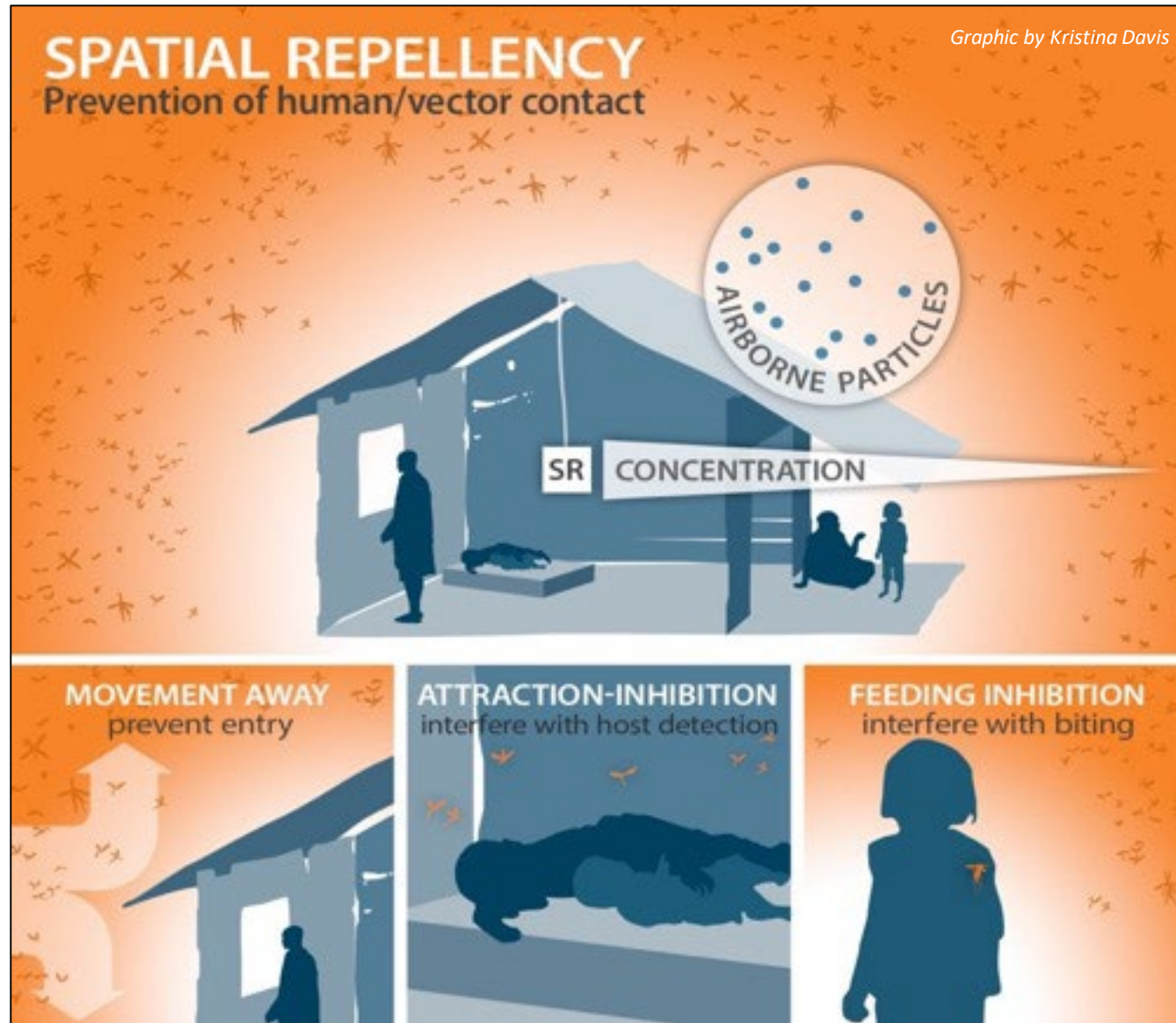


Spatial repellents: Roadmap to global recommendation of spatial repellents for public health use

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Spatial Repellents & Disease Control



Continuous release of active ingredient over time and space

Added Value

Addresses daytime, early-evening and indoor/outdoor vector biting

Varied modes of action

Innovation

New actives, alternate target sites, exploitation of post-exposure effects

Closing the Knowledge Gap on SR Public Health Value

Large-Scale Clinical Trials

Yunnan Province, CHINA & transfluthrin coils (0.03%)



PI: Nigel Hill, London School of Hygiene and Tropical Medicine

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HYGIENE
& TROPICAL
MEDICINE



Johnson
A Family Company

Coils vs Control = 77-80% PE ($p < 0.001$)

Sumba Island, INDONESIA & metofluthrin coils (0.00675%)



PI: Din Syafruddin, Eijkman Institute for Molecular Biology, Jakarta



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A Family Company

Coils vs Control = 60% PE ($p < 0.05$)

Hill et al. *Malaria Journal* 2014, 13:208
<http://www.malariajournal.com/content/13/1/208>



RESEARCH

Open Access

A household randomized, controlled trial of the efficacy of 0.03% transfluthrin coils alone and in combination with long-lasting insecticidal nets on the incidence of *Plasmodium falciparum* and *Plasmodium vivax* malaria in Western Yunnan Province, China

Nigel Hill^{1*}, Hong Ning Zhou^{1,2}, Piyu Wang², Xiaofang Guo², Iona Carneiro³ and Sarah J Moore^{3,4,5*}



THE AMERICAN JOURNAL OF
TROPICAL MEDICINE AND HYGIENE
official Journal of the American Society of
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Am J Trop Med Hyg. 2014 Dec 3; 91(6): 1079–1087.

doi: [10.4269/ajtmh.13-0735](https://doi.org/10.4269/ajtmh.13-0735)

PMCID: PMC4257627

PMID: [25311699](https://pubmed.ncbi.nlm.nih.gov/25311699/)

Impact of a Spatial Repellent on Malaria Incidence in Two Villages in Sumba, Indonesia

Din Syafruddin^{*}, Michael J. Bangs, Dian Sidik, Iqbal Elyazar, Puji BS Asih, Krisin Chan, Siti Nurleila, Christian Nixon, Joko Hendarto, Isra Wahid, Hasanuddin Ishak, Claus Begh, John P. Grieco, Nicole L. Aches, and J. Kevin Baird

Large-Scale Clinical Trials



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GATES foundation



Dengue Evaluation

Peru



UCDAVIS
UNIVERSITY OF CALIFORNIA



Thomas Scott, Amy Morrison et al.

Indonesia



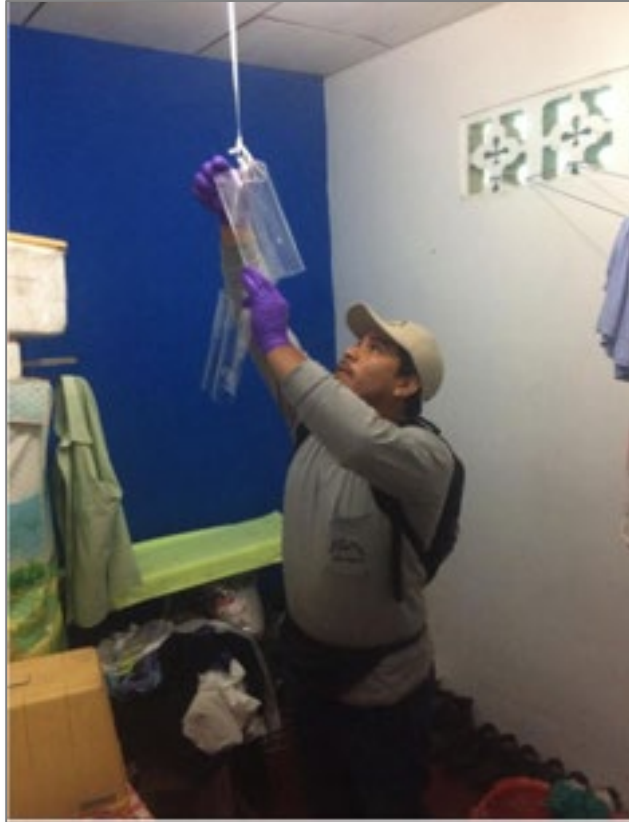
Malaria Evaluation



EIJKMAN INSTITUTE
for molecular biology

Din Syafruddin et al.

Passive Emanator – Transfluthrin* (2 week Duration)



**Transfluthrin is one of six registered 'spatial repellent' compounds commonly found in commercially available mosquito control products globally based on WHO specifications. The U.S. Environmental Protection Agency (EPA) recently approved transfluthrin products for indoor use (2018).*

Sumba Island, Indonesia- Primary Outcomes



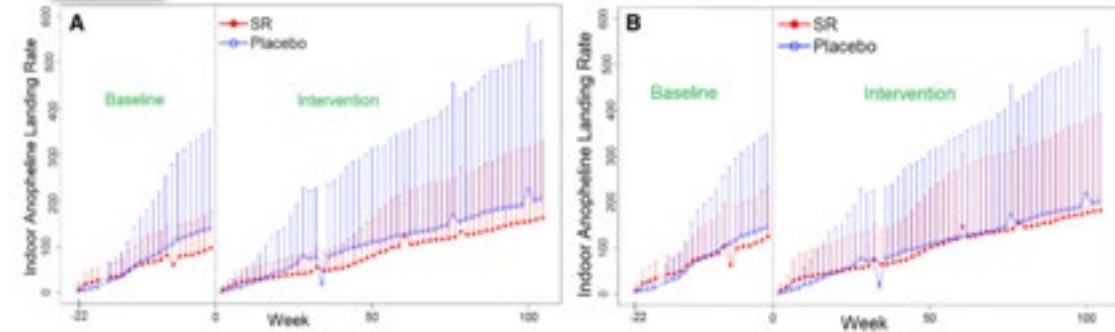
Am J Trop Med Hyg. 2020;102(5):344-358.
doi:10.4269/ajtmh.19-0554
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Efficacy of a Spatial Repellent for Control of Malaria in Indonesia: A Cluster-Randomized Controlled Trial

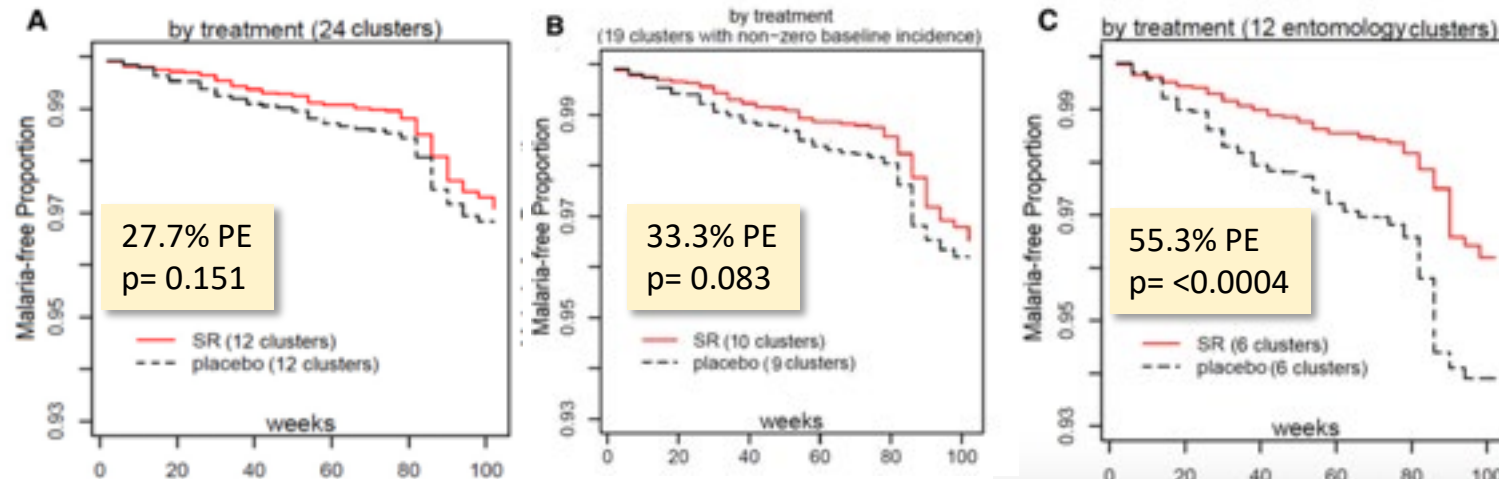
Din Syafruddin,^{1,2} Puji B. S. Asih,¹ Ismail Ekoprayitno Ruzi,¹ Dendi Hadi Permana,¹ Anggi Puspa Nur Hidayati,¹ Lopa Syahvanti,¹ Sri Zubaidah,¹ Dian Sidik,³ Michael J. Bangs,⁴ Claus Begh,⁵ Fang Liu,⁶ Evercita C. Eugenio,⁶ Jared Hendrickson,⁷ Timothy Burton,⁸ J. Kevin Baird,^{9,10} Frank Collins,¹¹ John P. Grieco,⁸ Neil F. Lobo,¹² and Nicole L. Achee¹³



16.4% and 11.3% reduction in anopheline attack rate indoors and outdoors, respectively.



Incidence (Time to First Infection)



Up to 65.6% PE ($p < 0.001$) in overall infection (first and all subsequent) in clusters with entomology collections.

Iquitos, Peru- Primary Outcomes

PNAS

RESEARCH ARTICLE

APPLIED BIOLOGICAL SCIENCES

OPEN ACCESS

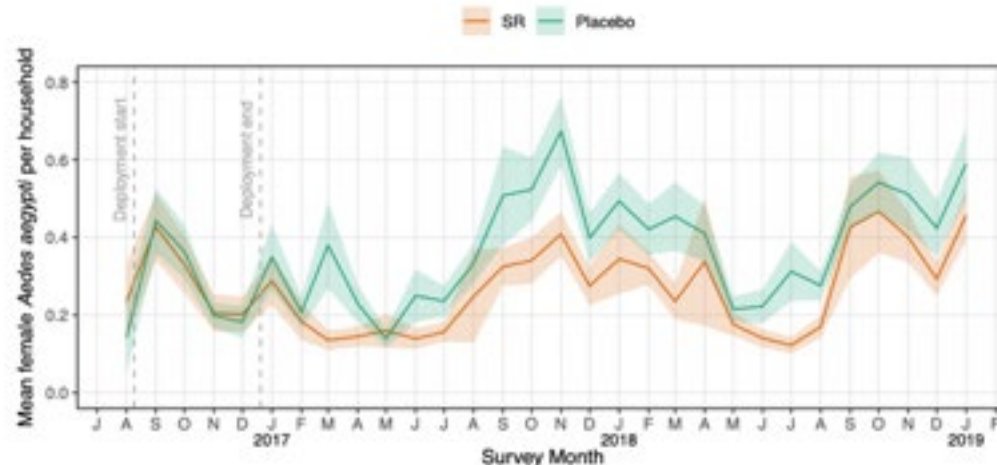
Efficacy of a spatial repellent for control of *Aedes*-borne virus transmission: A cluster-randomized trial in Iquitos, Peru

Amy C. Morrison^{AK1,†}, Robert C. Reiner Jr.^{5,†}, William H. Elson^{6,†}, Helio Azete⁷, Carolina Guevara^{8,9}, Clara del Aguila⁸, Isabel Bazar⁸, Crystyan Siles⁸, Patricia Barrera⁸, Anna B. Kawleki⁸, Christopher M. Barker⁸, Gisella M. Vasquez⁸, Karim Escobedo-Vargas⁸, Carmen Flores-Mendoza⁸, Alfredo A. Huaman⁸, Mariana Leguia⁸, Maria E. Silva⁸, Sarah A. Jenkins⁸, Wesley R. Campbell⁸, Eugenio J. Abente⁸, Robert D. Hontela⁸, Valerie A. Paz-Soldan⁸, John P. Grieco⁸, Neil F. Lobo¹⁰, Thomas W. Scott¹¹, and Nicole L. Achee^{1,2}

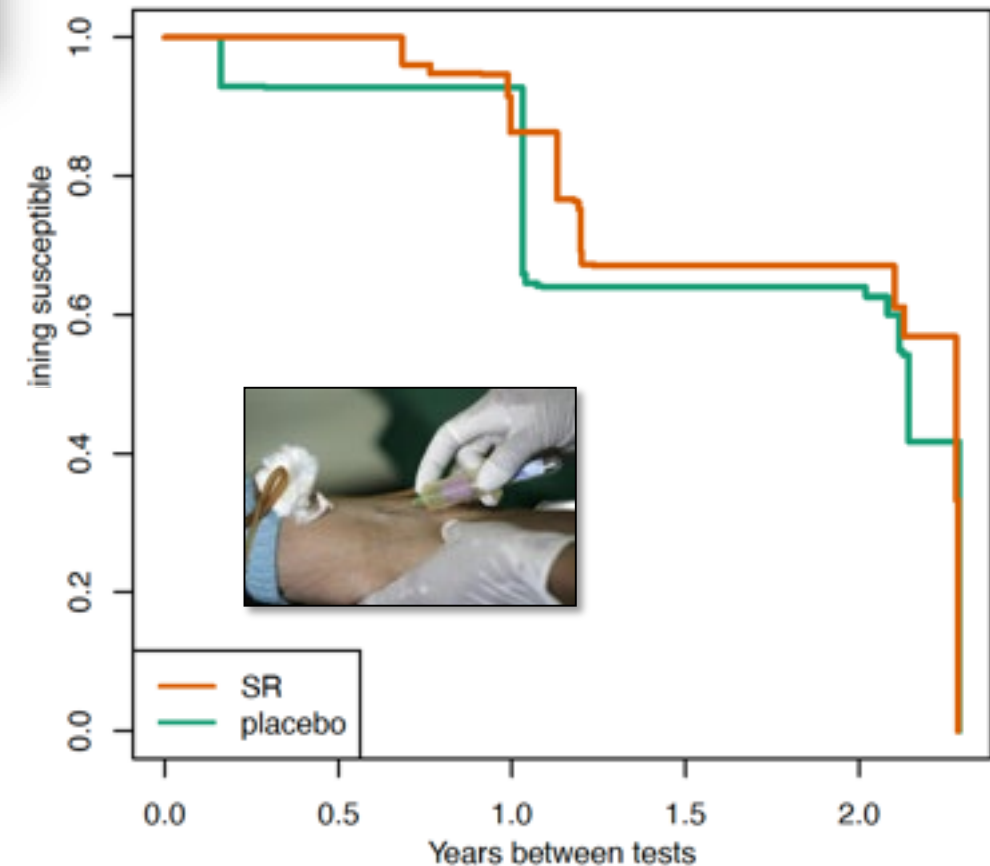
Edited by Anthony James, University of California, Irvine, CA; received October 6, 2021; accepted April 8, 2022



A 28.6% reduction in indoor adult *Ae. aegypti* female mosquito abundance, significantly different than control.

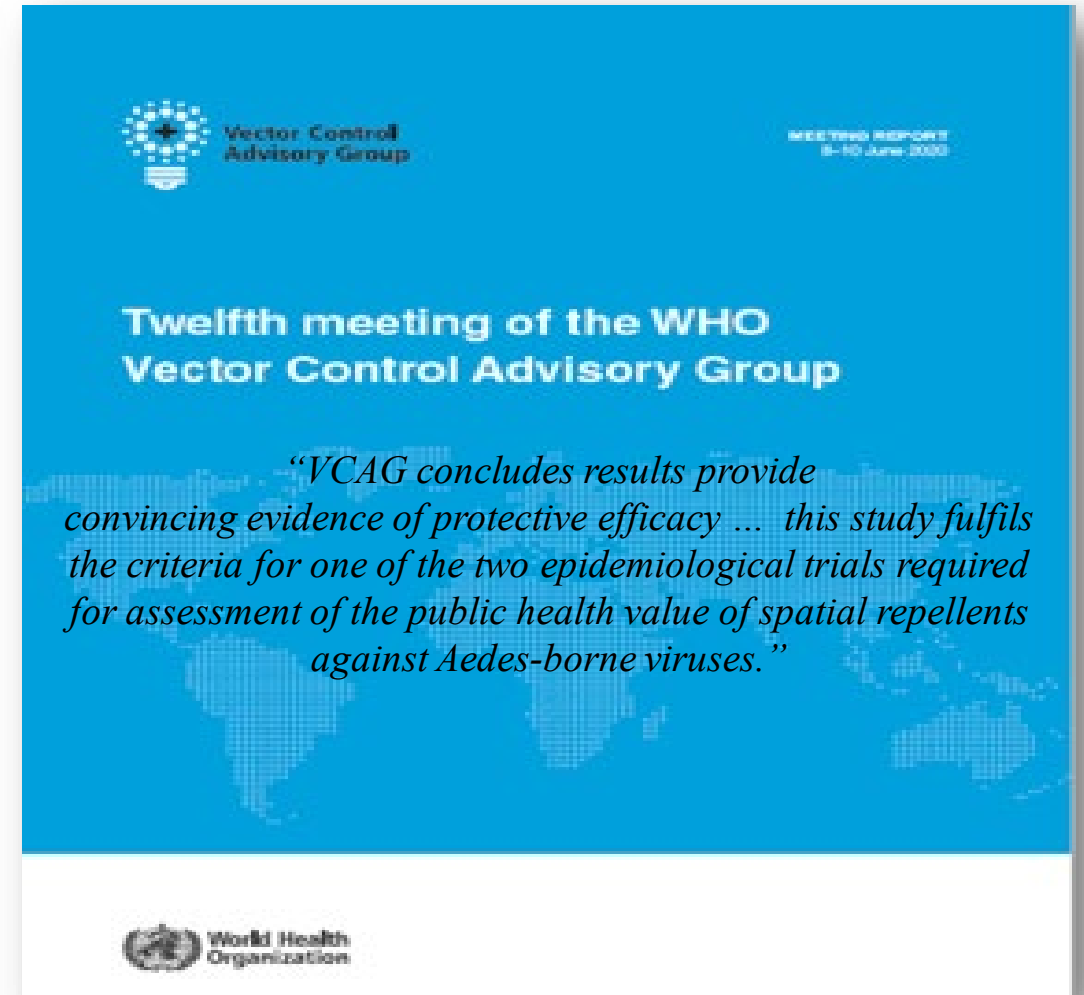
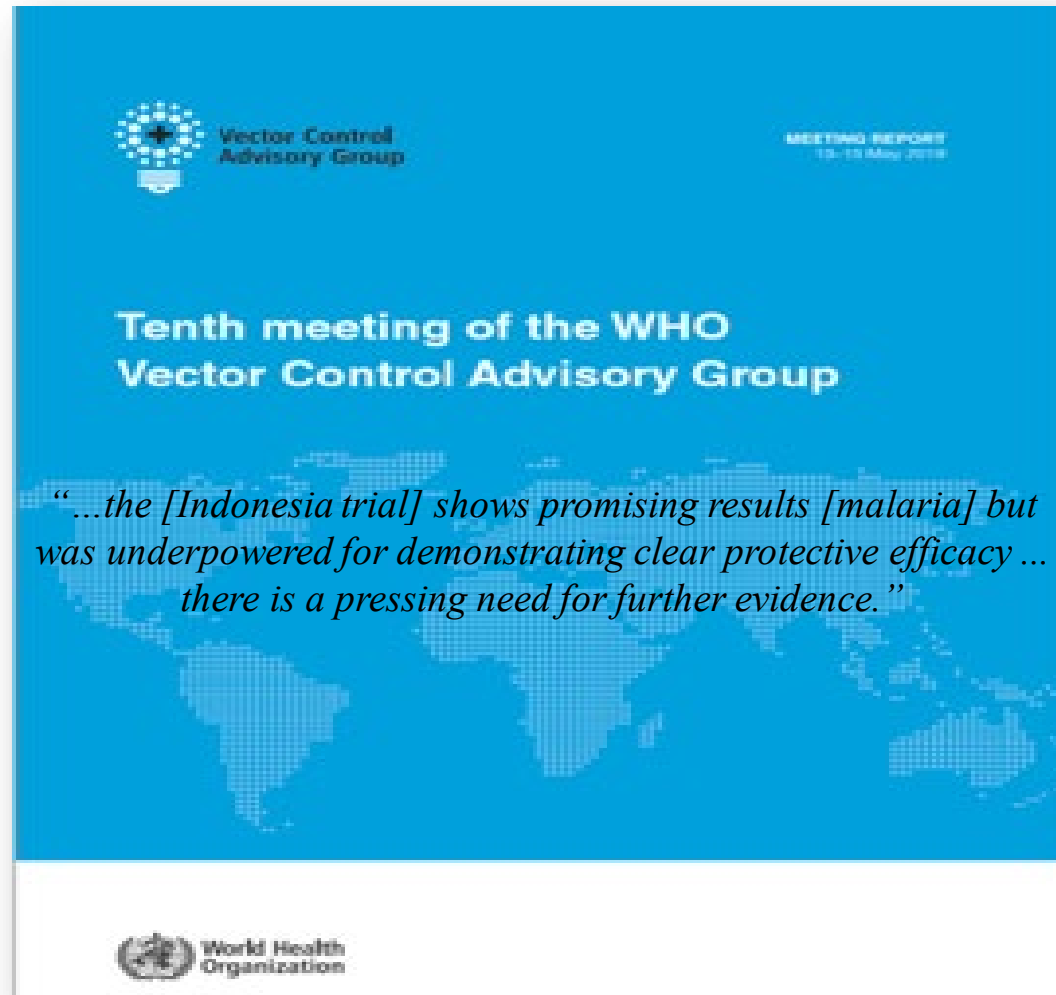


34.1% PE ($p=0.0236$) against ABV infection in subjects susceptible to Zika or wholly susceptible or monotypic to DENV

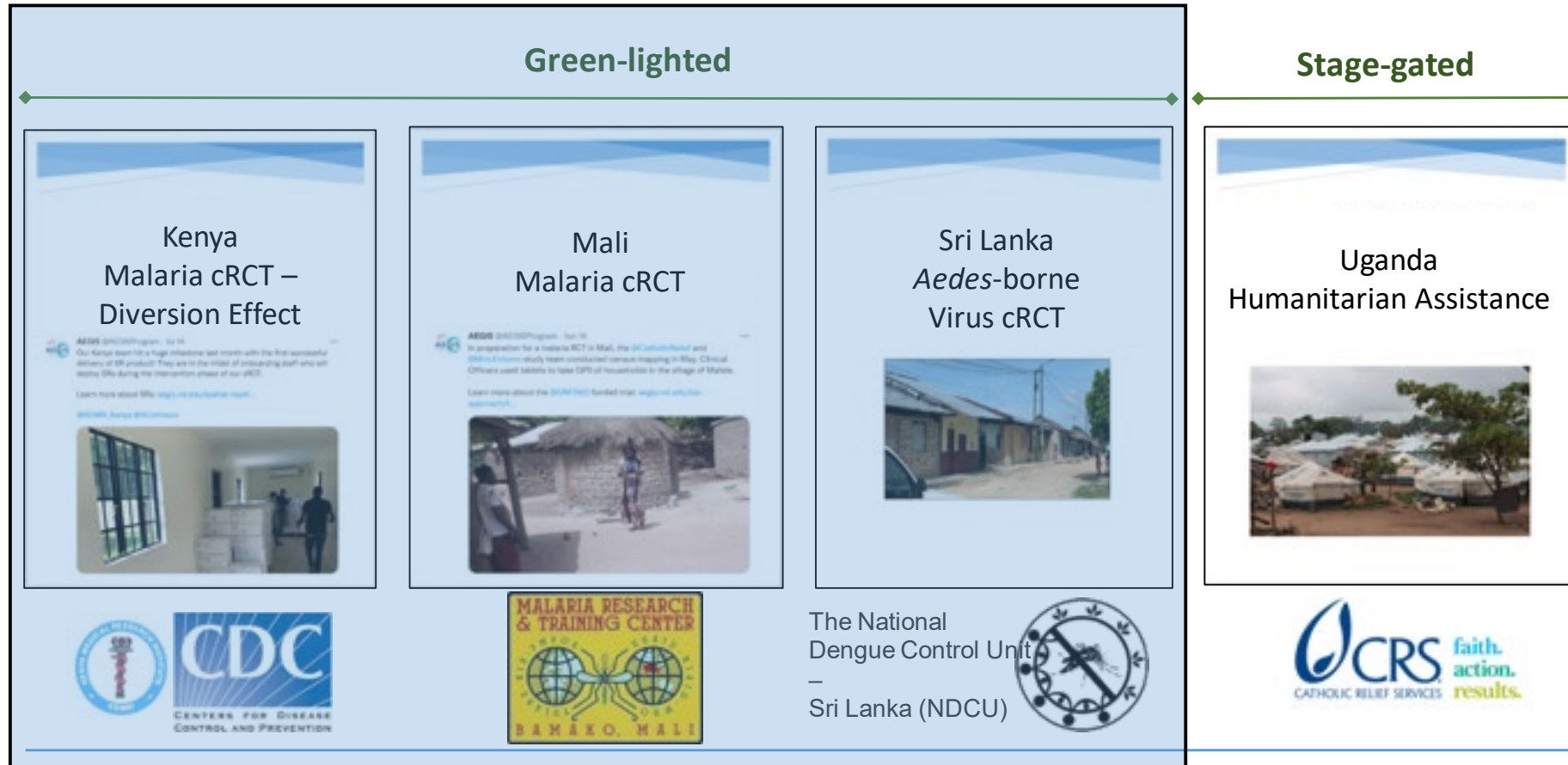


Trial Outcomes – WHO Public Health Value Assessment

Recommendations from Indonesia and Peru trials Posted in 10th and 12th VCAG Meeting Reports



Advancing the Paradigm



This project is made possible thanks to Unitaid funding and support. Unitaid finds new ways to prevent, treat and diagnose HIV/AIDS, tuberculosis and malaria more quickly, more cheaply and more effectively. It identifies innovative health solutions that show promise and invests in them to establish their viability so that partner organisations can then make them widely available. Unitaid addresses innovation barriers by supporting an integrated approach to health, accelerating the development and market introduction of better health products and by influencing the dynamics of the innovation landscape to benefit people in low resource settings.

Intervention – ‘MOSQUITO SHIELD™’ (4 week Duration)



Kenya Trial

Busia County, Teso South and North Subcounties

Eric Ochomo, John Gimnig et al.



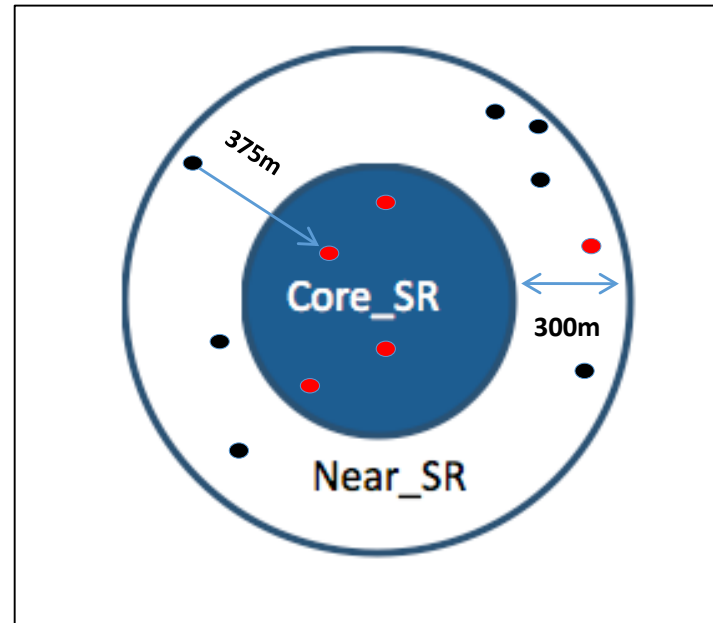
Study Site: Stable malaria, 2.5 - 4.1 infections/ppn/yr (Pf dominates). Widespread resistance to organochlorines and pyrethroids.

Epidemiology – 58 clusters (29 SR / 29 Placebo). Total of 2,162 subjects, 24mo follow-up. Two cohorts (≥ 6 mo-10yrs) with intervention in cluster 'cores' for estimates of PE, two cohorts without intervention in cluster 'buffers' for estimates of diversion.

Entomology – 20 clusters (10 SR / 10 placebo) to estimate impact of the SR on entomological measures using monthly CDC-Light Trap (indoor density) and quarterly indoor & outdoor human landing catches (HLC) in 12 clusters (6 SR / 6 Placebo).



Diversionary Effect / Community Effect



**Interim analyses on first time infections has been completed and results are currently being reviewed by Unitaid.*

Mali Trial

Sikasso Region, Kolondieba District

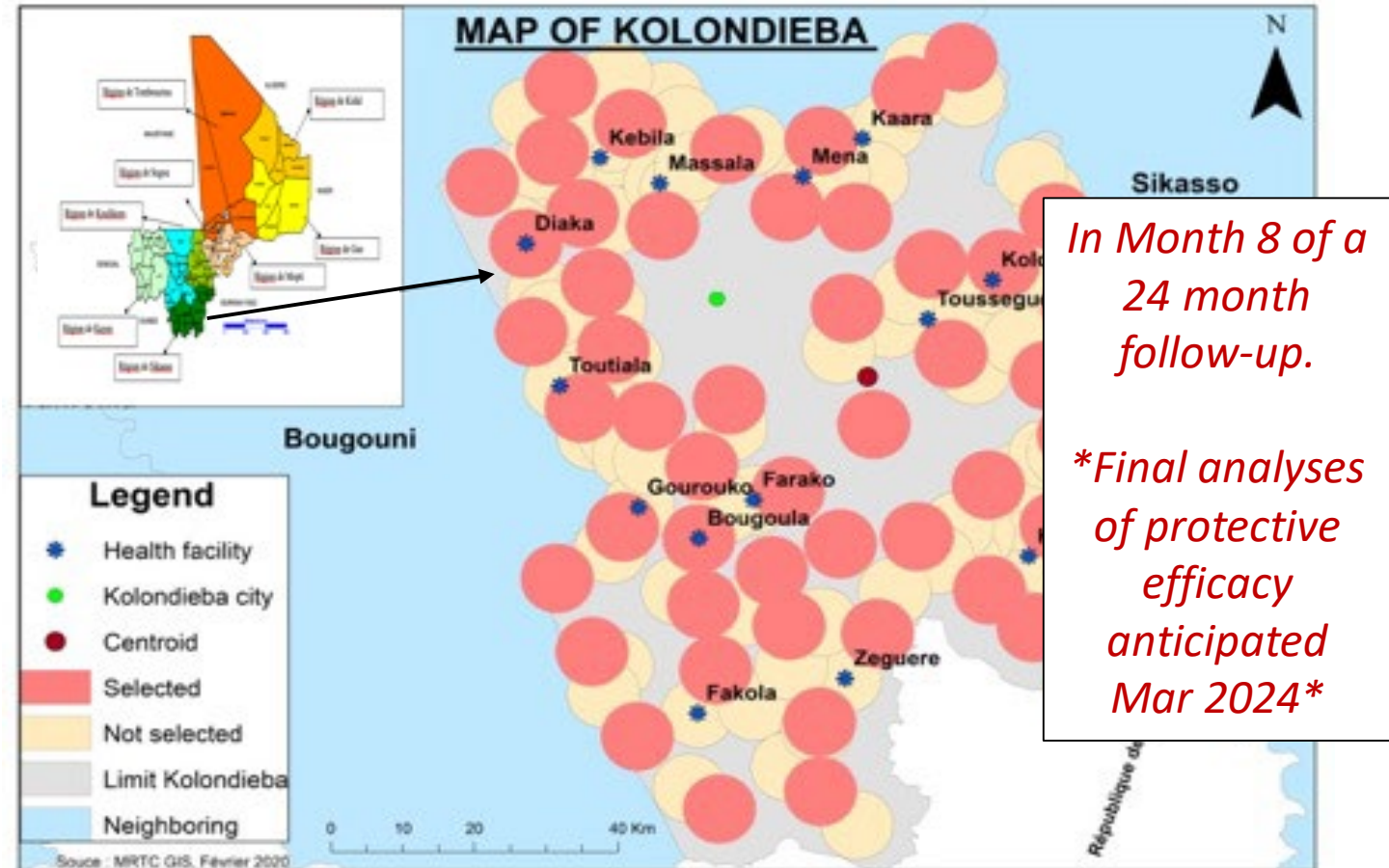
Issaka Sagara, Suzanne Van Hulle et al.



Study Site: Malaria transmission rates 205/1000 population in 2018 (*Pf* prevalence 29.7%). Documented resistance to pyrethroids, carbamates, organochlorines, organophosphates.

Epidemiology - 60 clusters (30 SR / 30 Placebo). Total of 1,920 subjects, 24mo follow up. Single cohort (≥ 6 mo-10 yrs) with intervention for estimates of PE.

Entomology - 20 clusters (10 SR / 10 Placebo) to estimate impact of the SR on entomological measures using monthly CDC-Light Trap (indoor density) (indoor density) and quarterly indoor / outdoor human landing catches (HLC) in 12 clusters (6 SR / 6 Placebo).



In Month 8 of a 24 month follow-up.

Final analyses of protective efficacy anticipated Mar 2024



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Sri Lanka Trial

Gampaha District, Negombo, Wattala and Kelaniya MoH Areas

Hasitha Tissera, Anoja Dheerasinghe et al.

The National Dengue Control
Unit – Sri Lanka (NDCU)



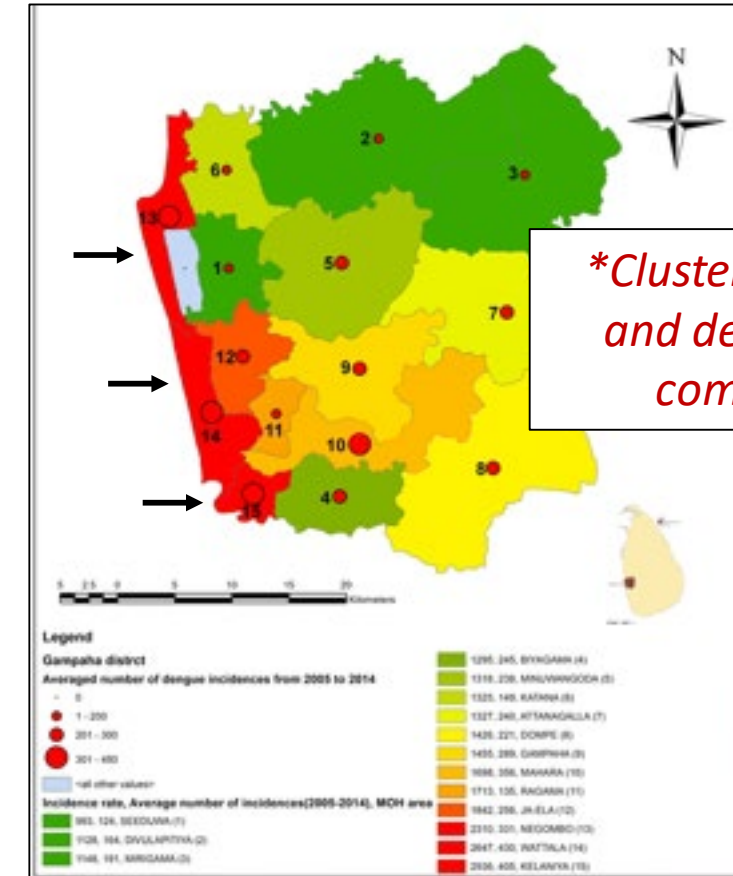
Study Site: Force of primary infection of 0.141 (case range 300-708 in 2018).

Epidemiology – 30 clusters (15 SR / 15 Placebo). Total of 19,747 subjects for febrile surveillance. A subset of ~3,900 <4-16 years for measuring dengue virus infection – the ‘longitudinal cohort’ – based on seroconversion against Dengue, Chikungunya, Zika (DCZV). 24mo followup.

Entomology - All participating houses will be monitored entomologically using Procopak aspiration to capture indoor *Aedes aegypti* prior to deployment and then 1x month during intervention to estimate impact on *Ae. aegypti* population densities and blood fed status.



Withanage, G. P. et al., (2020). PloS One, 15(5), e0231408.



Withanage, G.P., et al., (2018). Parasites Vectors 11, 262.



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Operational Use Trial

Bidibidi Refugee Camps in Yumbe, Uganda

Suzanne Van Hulle, Momar Mbodji et al.

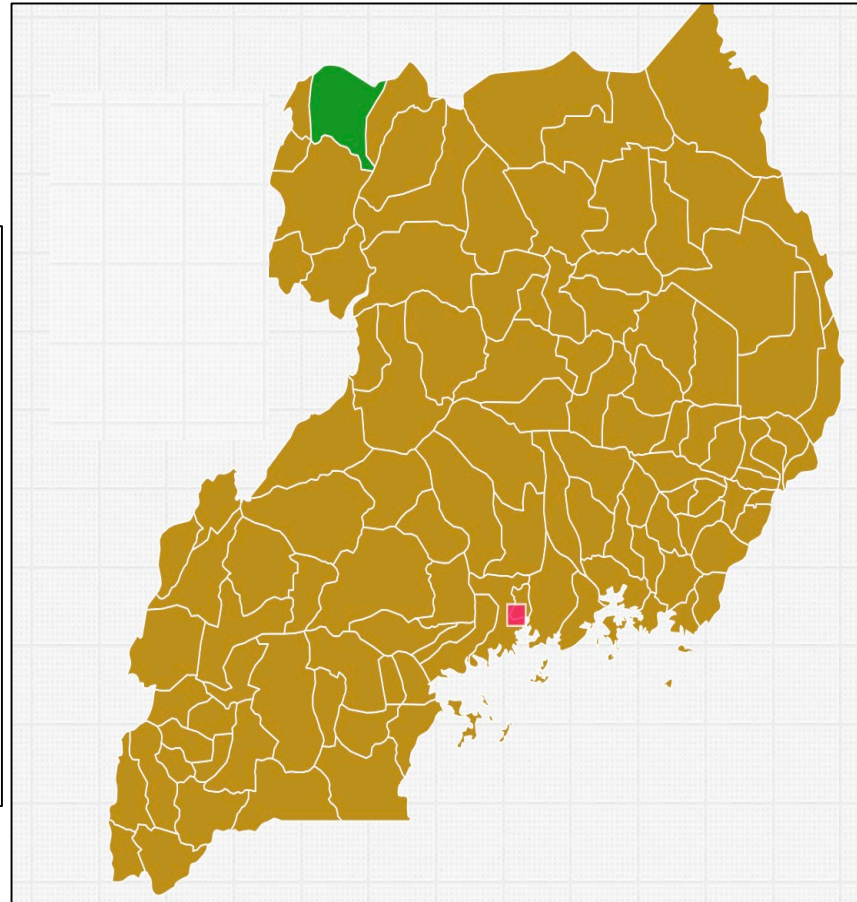


Design: Evaluate the protective efficacy (PE) of spatial repellent (SR) on malaria in pregnant women and children under five

Epidemiology –

3 study arms:

- Reference Arm - Study Team Delivered – 16 clusters
- Community Health Worker Delivery – 16 clusters
- Voucher System – 16 clusters
- GOAL – determine the most appropriate delivery method for rapid roll out.



**Trial awaits a green light based on Kenya interim analysis*

*Anticipated completion by Q4 of 2024**



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Advancing SR Products Towards Public Health Use



2014-2019

- Sealed film that emanates once opened, for a **2-week** duration of protection indoors.
- Product evaluated in clinical trials in Indonesia and Peru.



2019-Present

- Improved version of 2-week product that provides **1-month** of protection indoors.
- Currently being evaluated in clinical trials in Kenya, Mali, and Sri Lanka.
- Both malaria trials scheduled to be completed by March of 2024.



Next Steps

- Awaiting green light for operational trials to be conducted in displaced person camps in Uganda.



Optimal distribution channels and cost-effective for operational implementation

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