

Non-inferiority of Guardian™ compared to Mosquito Shield™

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Volatile pyrethroid spatial repellents (VPSR) as public health intervention

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Efficacy of a Spatial Repellent for Control of Malaria in Indonesia: A Cluster-Randomized Controlled Trial

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Ochomo et al. *Trials* (2022) 23:260
<https://doi.org/10.1186/s13063-022-06196-x>

Trials



Eighteenth meeting of the WHO Vector Control Advisory Group

Meeting report, 24–26 April 2023

STUDY PROTOCOL

Open Access

Evaluation of the protective efficacy of a spatial repellent to reduce malaria incidence in children in western Kenya compared to placebo: study protocol for a cluster-randomized double-blinded control trial (the AEGIS program)



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Study aim



To assess the non-inferiority of **Guardian™**, a 12 month-product compared to **Mosquito Shield™**, a 1-month product using standard WHO phase II experimental hut testing method

Method



Treatment arms

- ~ Mosquito Shield™ vs Negative control
- ~ Guardian™ vs Negative control

Study design

- ~ 8 huts per arm for Guardian™ (N= 768)
- ~ 4 huts per arm for Mosquito Shield™ (N= 128)
- ~ each product was evaluated for its full duration of efficacy

Study duration

	2022								2023				
	M	J	J	A	S	O	N	D	J	F	M	A	M
Guardian													
Shield													

Method

~ Experimental huts (28m³) ; male volunteers

~ One shift: 18:00 – 06:00 h

~ Collections: inside-net, resting on wall & floor, and window exit-traps

Primary endpoint

~ Number of *Anopheles arabiensis* mosquitoes blood-fed

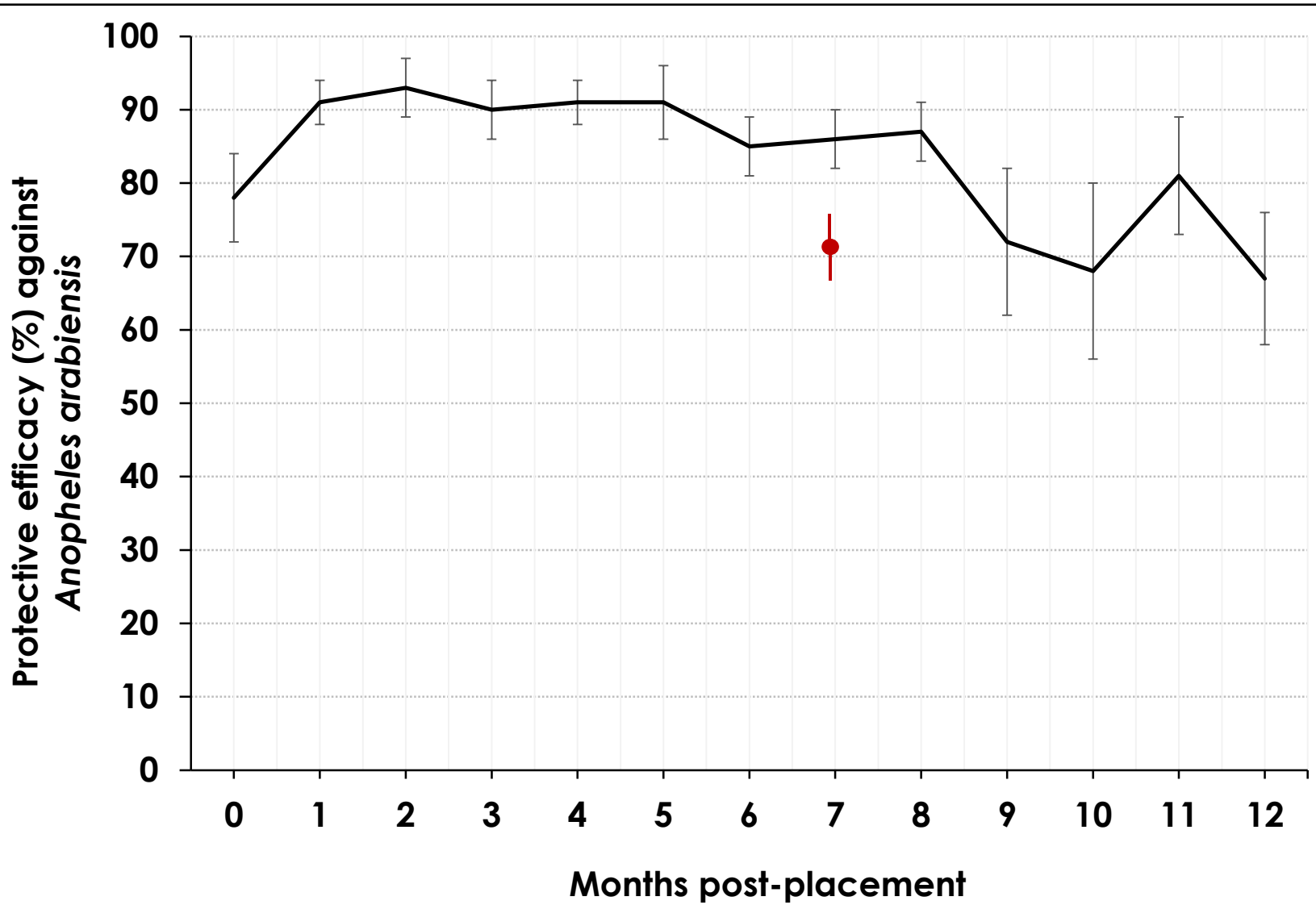
Secondary endpoints

~ Proportion of *Anopheles arabiensis* mosquitoes blood-fed

~ Proportion of *Anopheles arabiensis* mosquitoes dead at 24 hours



Efficacy of Guardian™ in reducing blood-feeding



Overall for Guardian™
~ 83% (78 – 86%); $p < 0.001$

Overall for Mosquito Shield™
~ 71% (65 – 76%); $p < 0.001$

Analysis

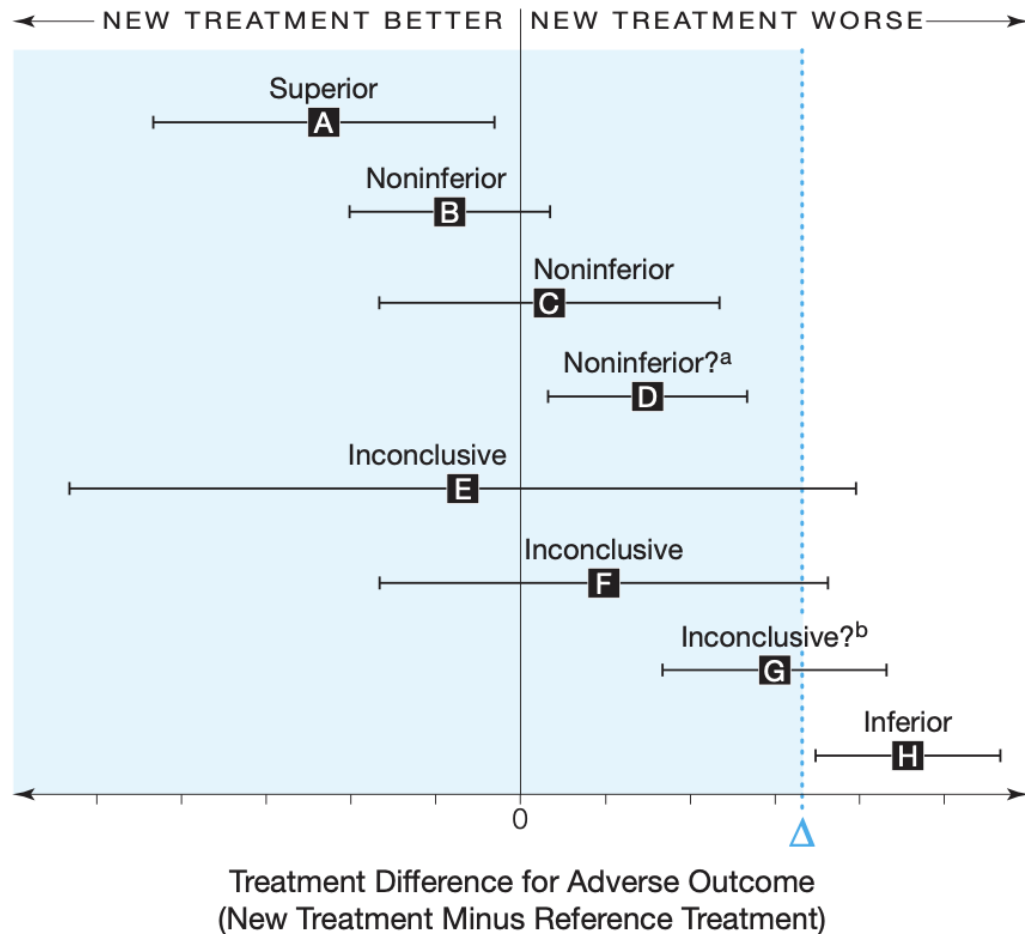
- ~ The WHO has set the non-inferiority margin at 7%
- ~ Analysis using regression models controlling for treatment volunteer study and date as fixed effects, huts as random effects since the treatments were fixed all throughout the study
- ~ Estimated odds ratio or a rate ratio that corresponds to a 7% difference relative to the outcome in the reference product

Results

	Mosquito Shield™		Guardian™	
<i>Anopheles arabiensis</i>	Control	Intervention	Control	Intervention
N females entering	4,577	3,205	26,930	12,863
N females blood-fed (BF)	1,347	402	7,297	1,596
N females BF per hut night	6.7 (5.6, 8.1)	1.9 (1.5, 2.3)	5.5 (5.1, 6.0)	0.9 (0.8, 1.0)
% reduction in number BF		71 (65, 76)		83 (79, 86)
% BF (95%CI)	34 (30, 38)	14 (11, 17)	39 (28, 31)	13 (11, 114)
% reduction in proportion BF		64 (59, 70)		67 (64, 69)
N females dead	11	746	74	2,170
% 24-hour mortality (95% C.I.)	0.3 (0.1, 0.5)	26 (22, 30)	0.5 (0.2, 0.6)	20 (18, 22)

Interpretation

Figure 1. Possible Scenarios of Observed Treatment Differences for Adverse Outcomes (Harms) in Noninferiority Trials



**Reporting of Noninferiority
and Equivalence Randomized Trials**
Extension of the CONSORT 2010 Statement

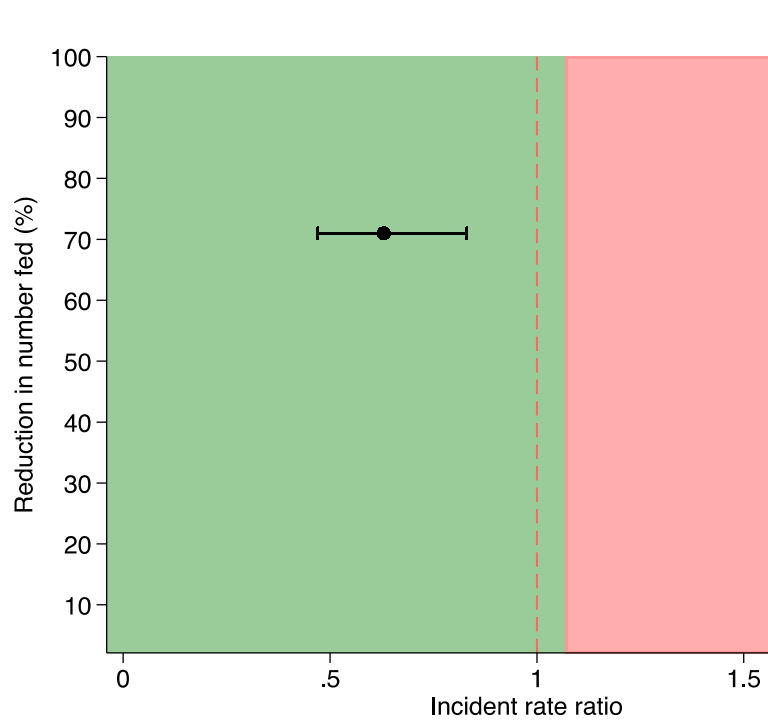
Piaggio et al JAMA. 2012;308(24):2594-2604

Non-inferiority results

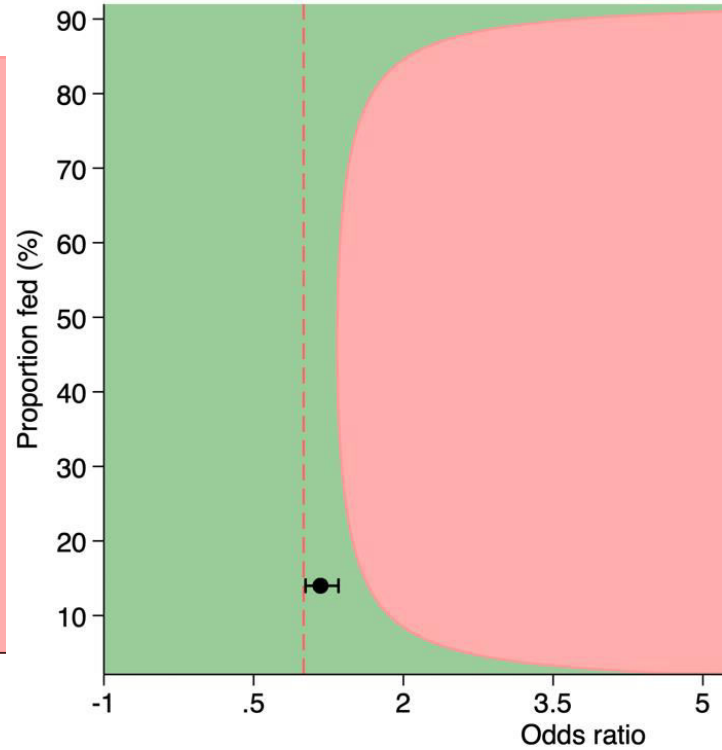
Outcome	Reference	Candidate	delta	OR	CI	Test outcome
Primary: Number blood fed	Mosquito Shield™	Guardian™	1.07	0.63	0.47, 0.83	Non-inferior and superior
Secondary: Proportion Blood fed			1.63	1.17	1.02, 1.35	Non-inferior
Secondary Proportion dead			0.54	0.71	0.22, 2.27	Indeterminate result

Non-inferiority results

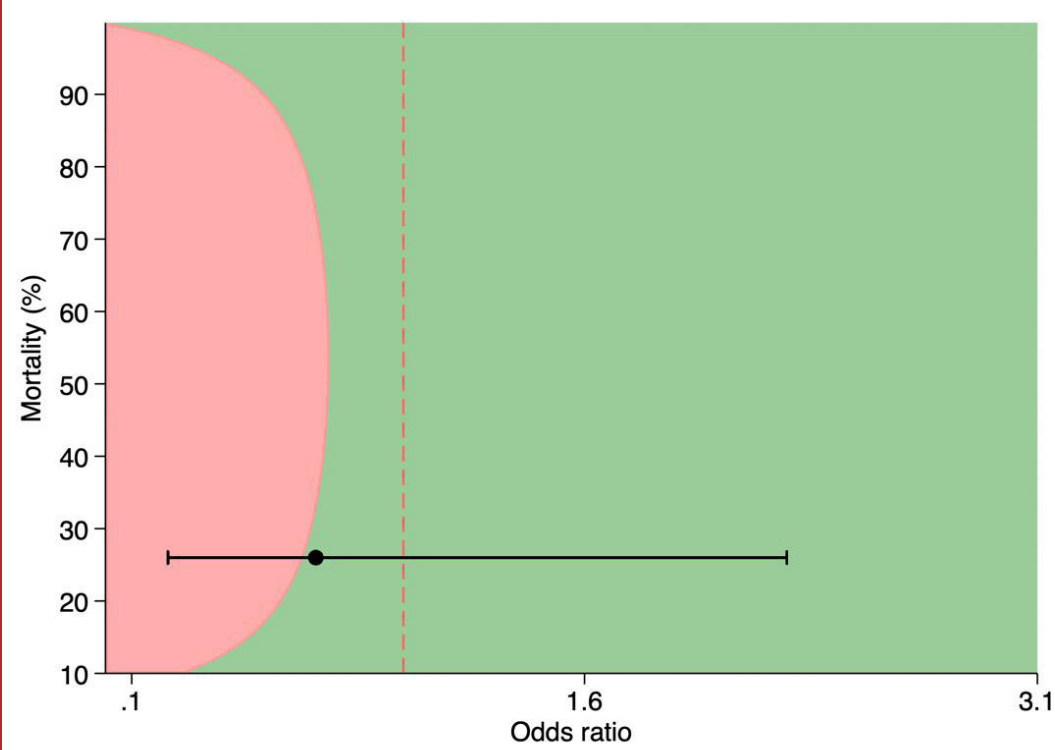
Number blood fed



Proportion blood fed



Proportion dead



Conclusion

~ Tested continuously for 12 months Guardian™ was non-inferior and superior to Mosquito Shield™ tested for 32 days on the primary endpoint of number of blood fed mosquitoes

~ Guardian™ was also non-inferior to Mosquito Shield™ on the secondary endpoint of proportion of blood fed mosquitoes

~We propose this a method for non-inferiority evaluations of spatial repellents



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