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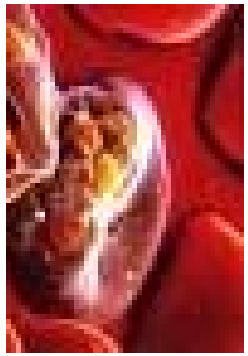
Moderate efficacy malaria vaccines as part of comprehensive malaria control and elimination



Progress and Limitation of Existing Vector Control Tools

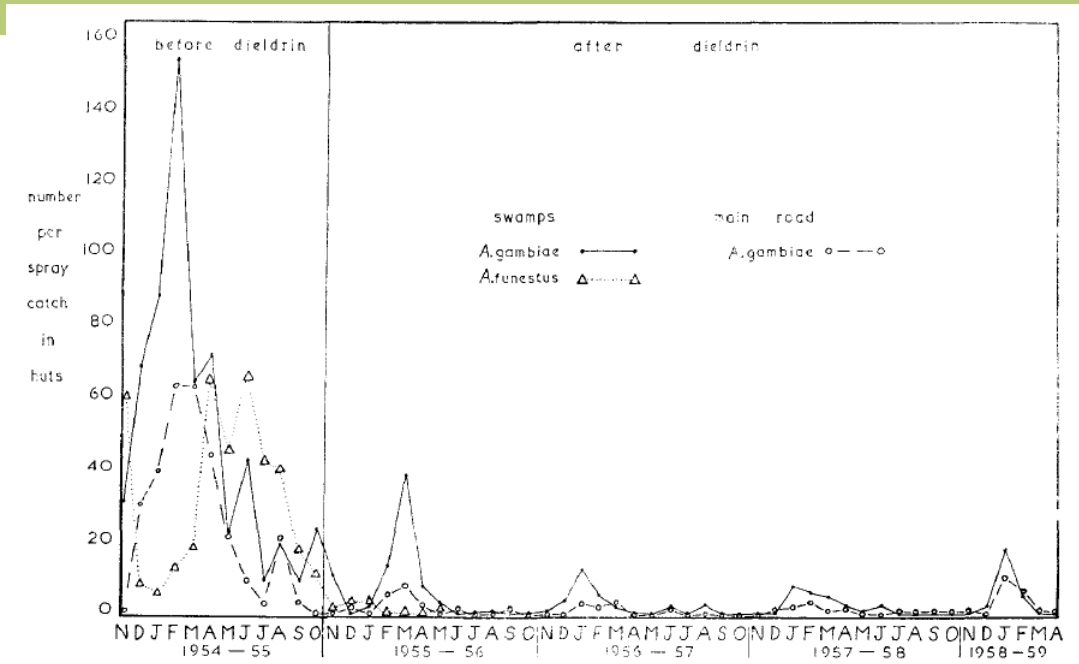
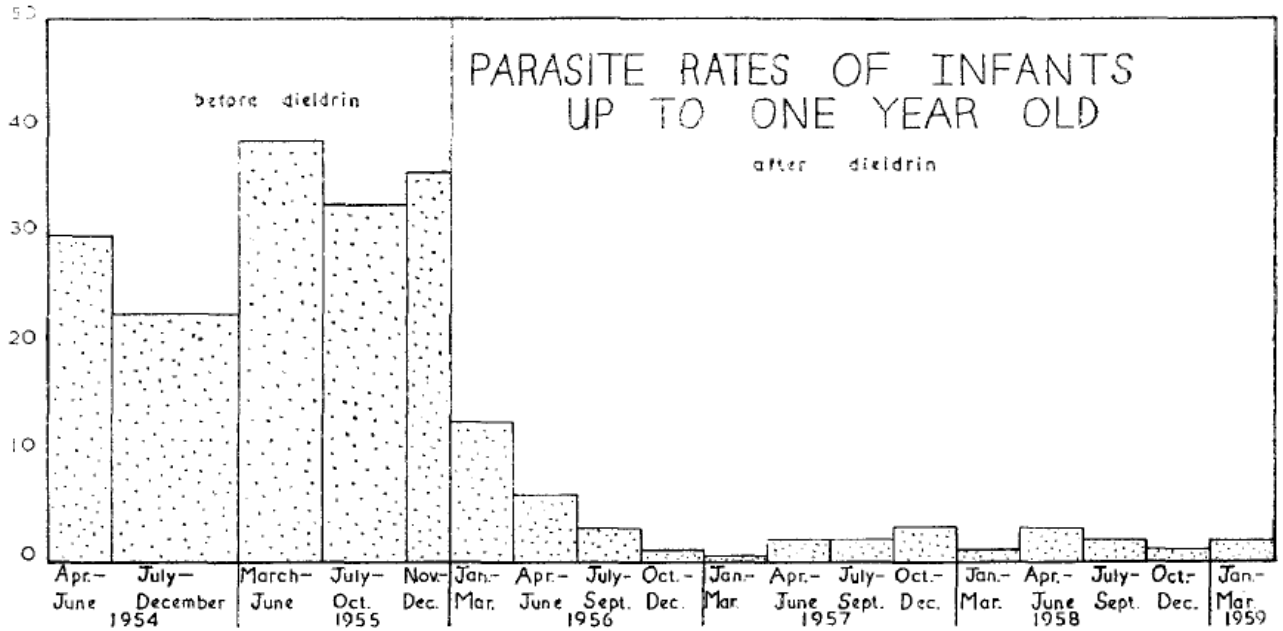


FIG. 1. Numbers of *A. gambiae* and *A. funestus* in spray catches in huts.



Draper & Smith 1960 TRSTMH 54: 342

Cannot afford to stop

Cohen et al. Malaria Journal 2012, 11:122
http://www.malariajournal.com/content/11/1/122

MALARIA JOURNAL

RESEARCH Open Access

Malaria resurgence: a systematic review and assessment of its causes

Justin M Cohen[1*], David L Smith[2,3], Chris Cotter[4], Abigail Ward[1], Gavin Yamey[4], Oliver J Sabot[1] and Bruno Moonen[1]

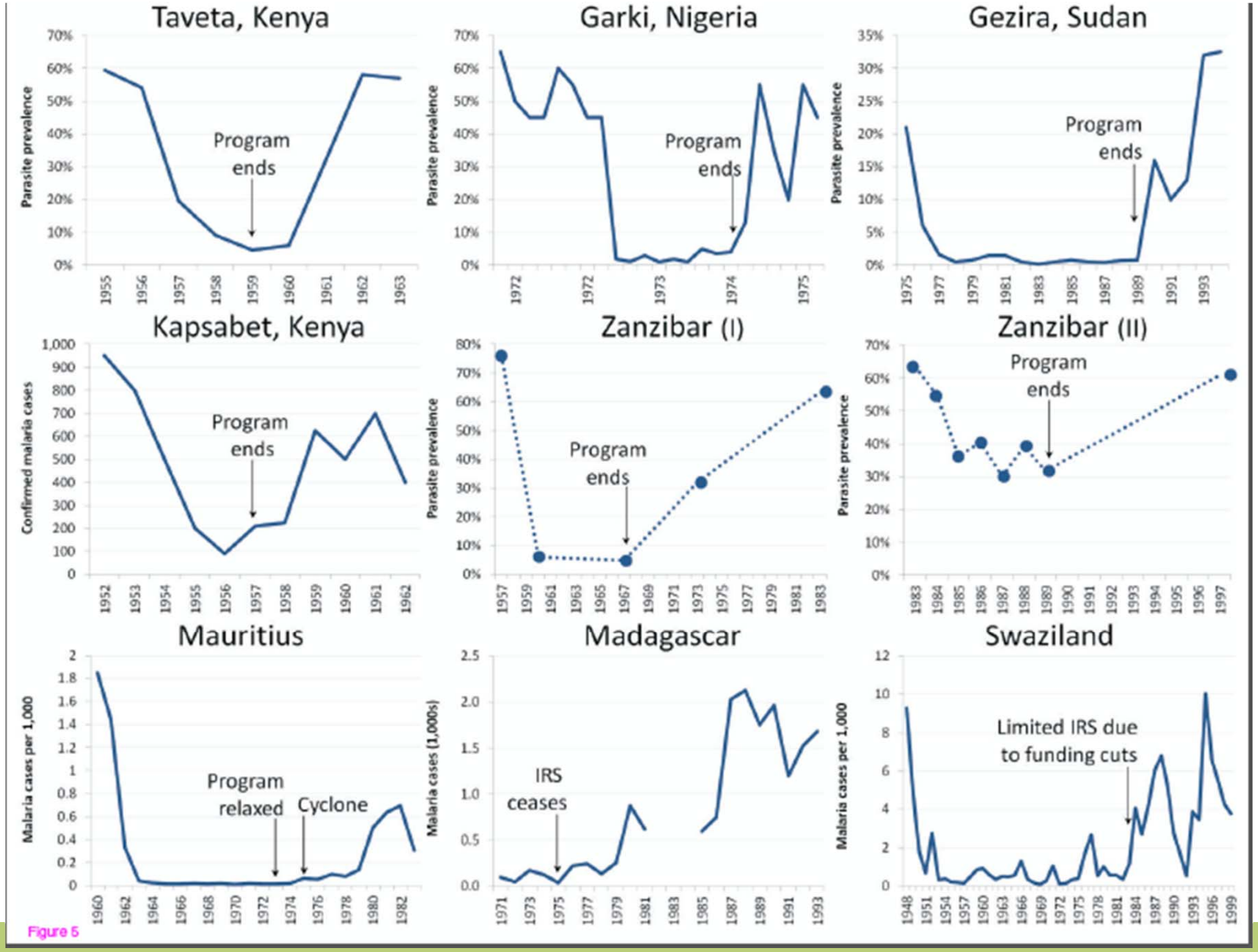


Figure 5

Global malaria vaccine pipeline

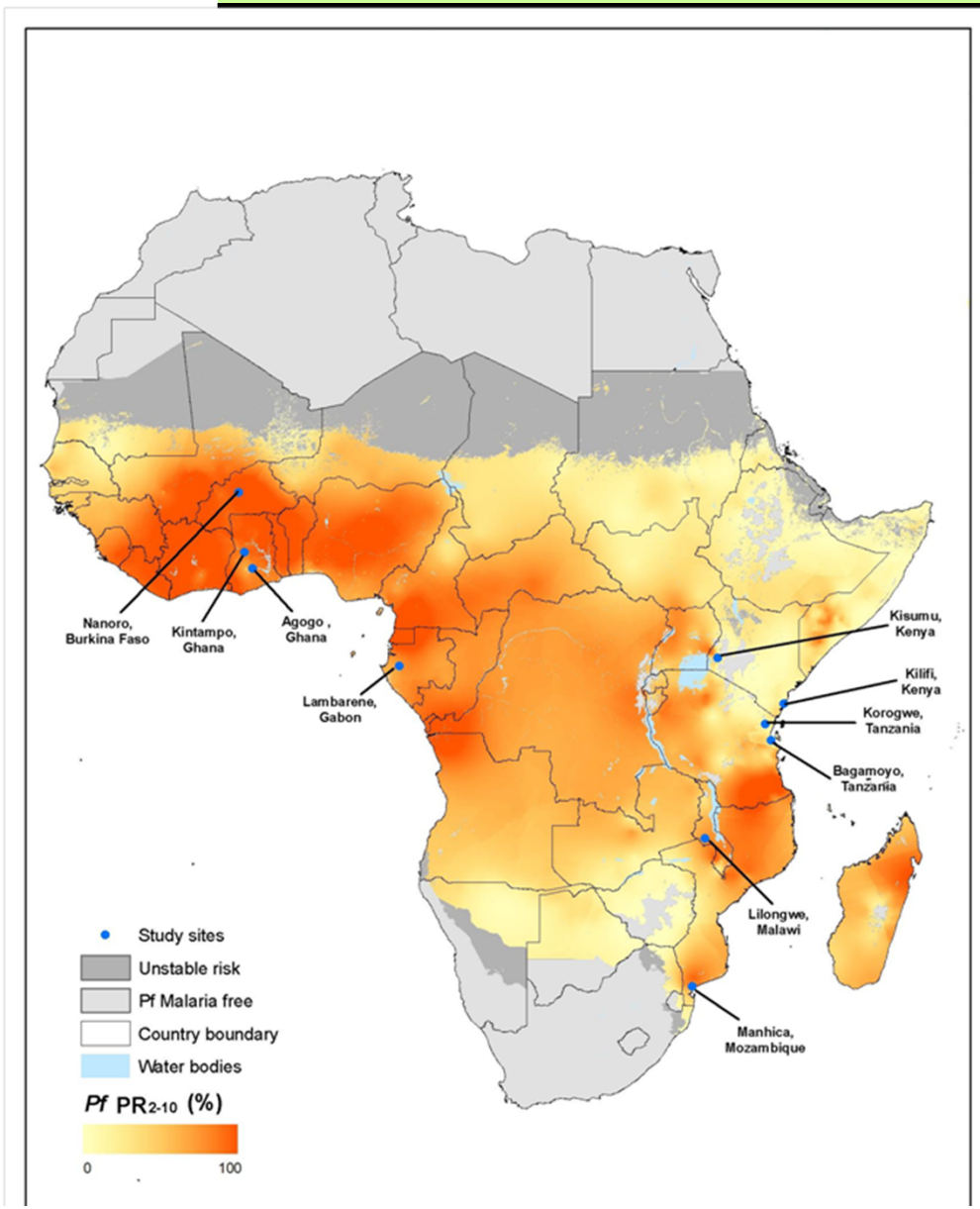
TRANSLATIONAL PROJECTS			VACCINE CANDIDATES		
Phase 1a	Phase 2a		Phase 1b	Phase 2b	Phase 3
ChAd63/MVA ME-TRAP + Matrix M™	Ad35.CS/ RTS,S-AS01	M3V.Ad.*Pf*CA	Ad35.CS	ChAd63/MVA ME-TRAP	RTS,S-AS01
Polyepitope DNA EP 1300	Ad35.CS/ Ad26.CS	M3V.D/ Ad.*Pf*CA	EBA 175.R2	GMZ2	
PfCelTOS FMP012	ChAd63/ MVA (CS, TRAP, AMA)	ChAd63/MVA MSP 1	SE36	MSP3 [181-276]	
CSVAC		ChAd63.AMA1/ MVA.AMA1	*Pf*SPZ		
ChAd63.AMA/ MVA.AMA1 +AI/CPG7909		FMP2.1-AS01B (AMA1 3D7)			
SR11.1					
ChAd63/MVA PvDBP					
*Pfs*25-EPA					
*Pfs*25-VLP					

***P. falciparum* vaccines:** Pre-erythrocytic | Blood-stage | Transmission-blocking

***P. vivax* vaccines:** Pre-erythrocytic | Blood-stage | Transmission-blocking

Data source: http://www.who.int/vaccine_research/links/Rainbow/en/index.html

RTSS Phase 3 Trial in Africa



Randomized, controlled, double-blind trial designed to evaluate vaccine efficacy, safety, reactogenicity, and immunogenicity in children up to 32 months after the administration of the first dose of vaccine.

Two age categories:

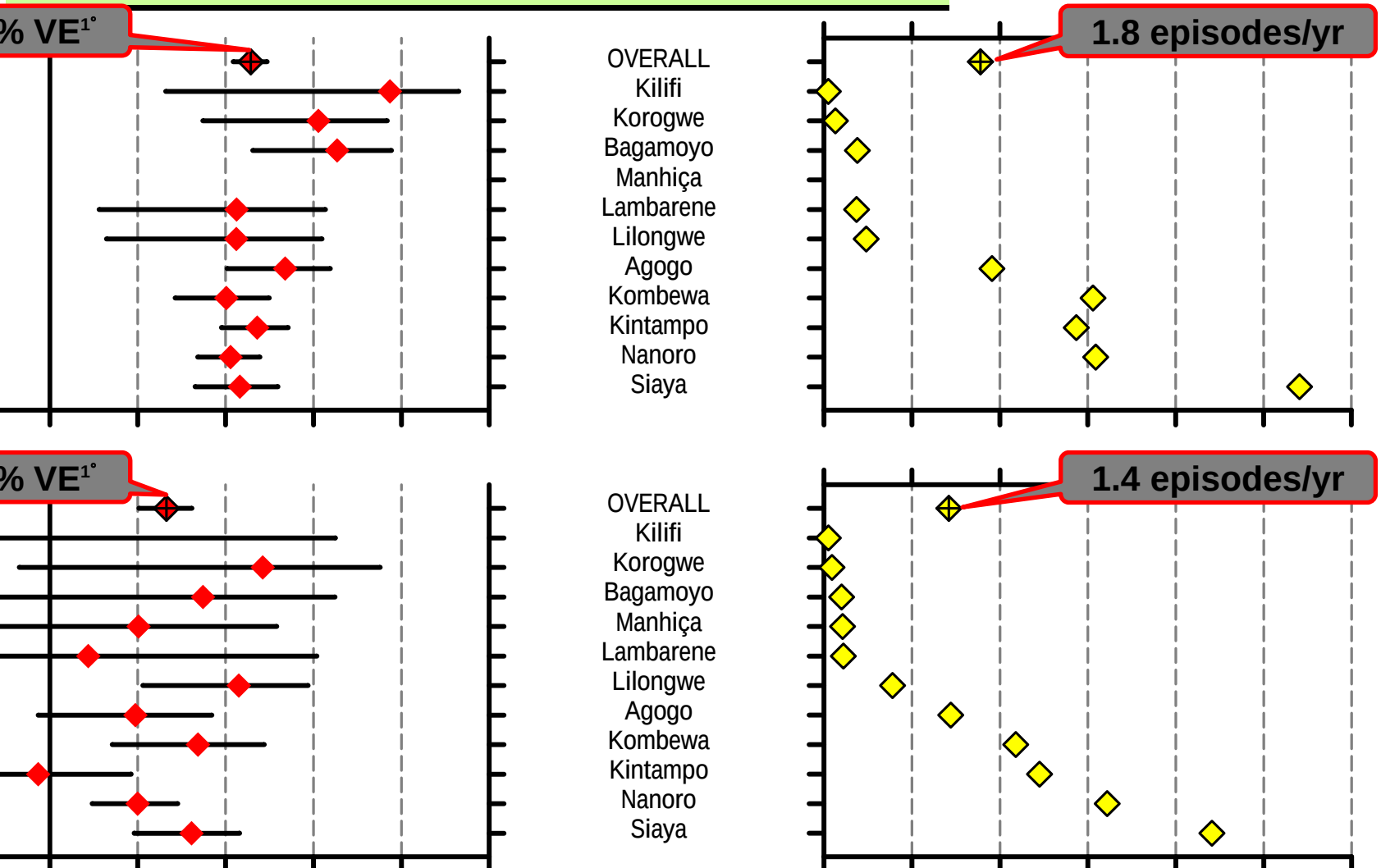
- Children 6-12 weeks of age: **7100**
- Children 5-17 months of age: **8900**

11 centers in 7 African countries

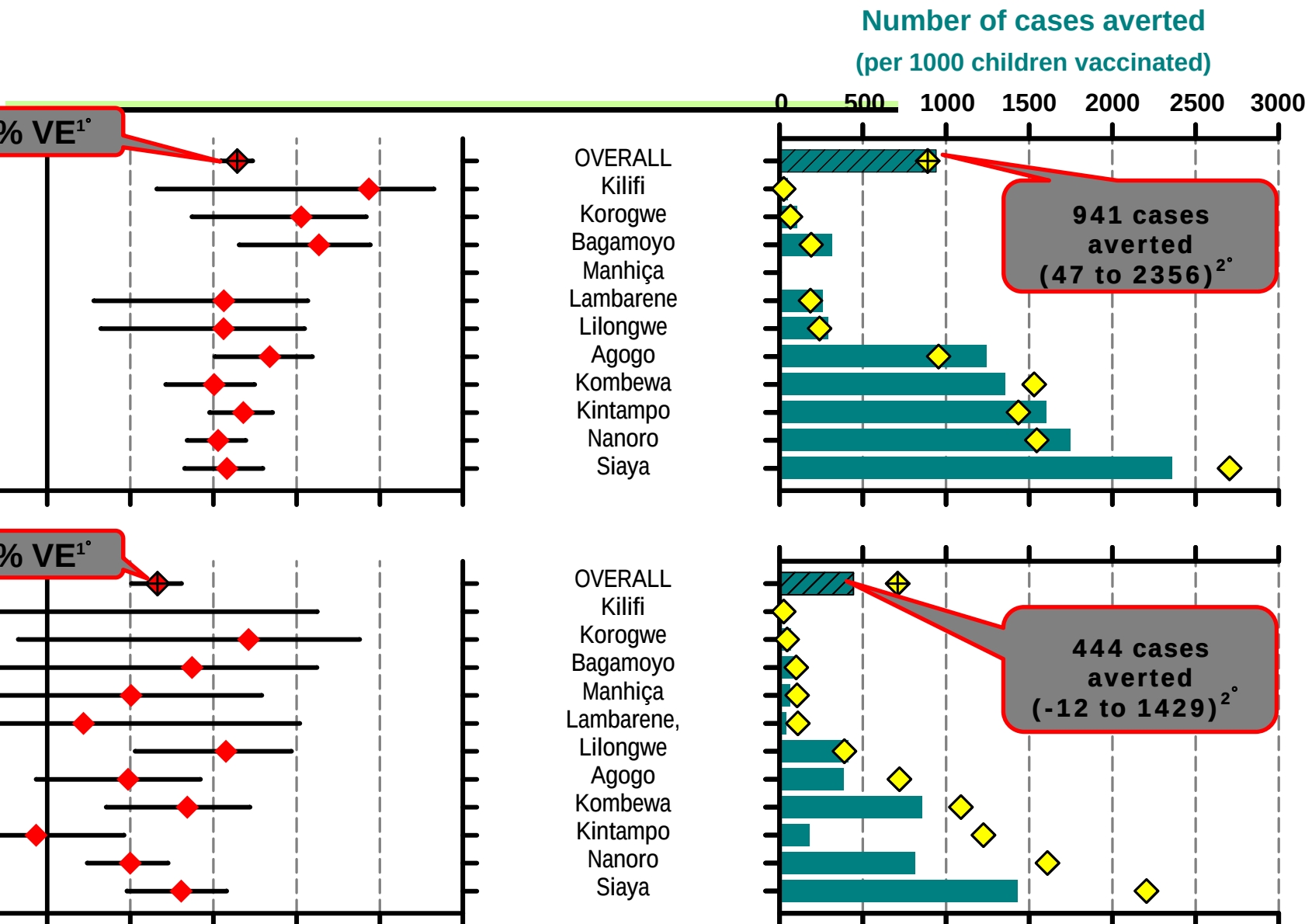
Trial implemented with optimized vector control and malaria treatment

The co-primary endpoints of the trial are: vaccine efficacy against clinical malaria after 12 months of follow-up in each age category.

ne Efficacy over 18 months follow-up [ATP] and Malaria ence in Controls



ct of RTS,S/AS01 on clinical malaria over 18 months of follow-



gainst severe malaria, malaria hospitalization all-cause hospitalization over 18 Months

	VE* in children [95%CI]	VE* in infants [95%CI]
ere malaria	**36%** [15 – 51]	**15%** [0 – 39]
aria hospitalization	**42%** [29 – 52]	**17%** [-7 – 36]
cause pitalization	**19%** [9 – 28]	**6%** [-7 – 17]

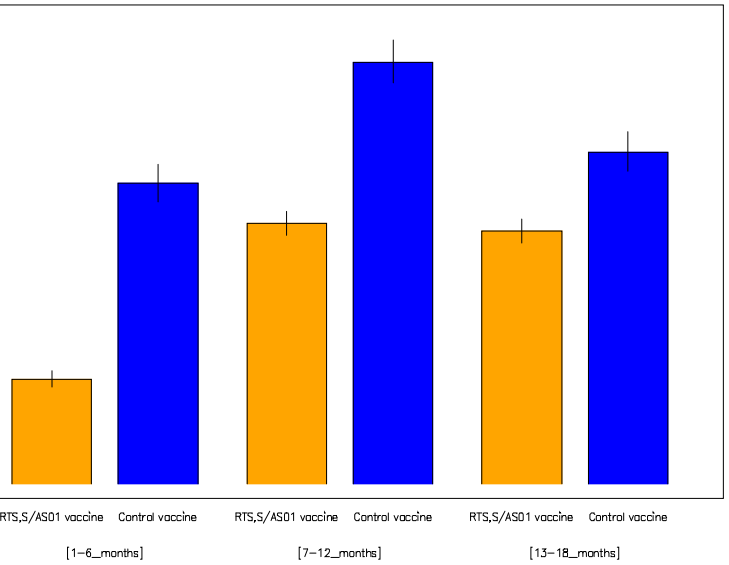
alculated as 1-Risk Ratio (Unadjusted)

er 18 months per 1000 vaccinees; **RTS,S/AS01** erted **21** [range:-4-44] **cases** and **8** [range:-14-33] **ses of severe malaria** in children and infants spectively.

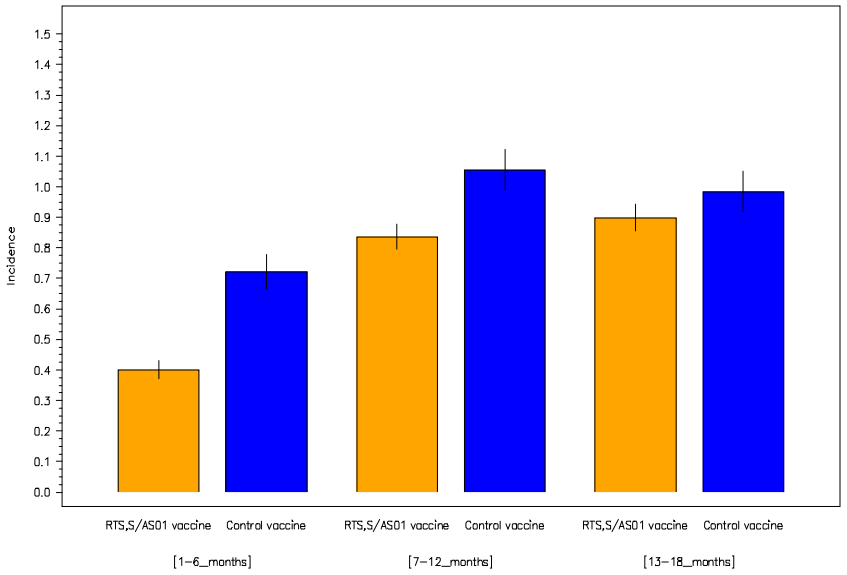
se fatality rate for malaria and **all-cause ortality** was low and **VE was not demonstrated**

incidence of clinical and severe malaria (primary case ons) by 6-month periods (per-protocol population)

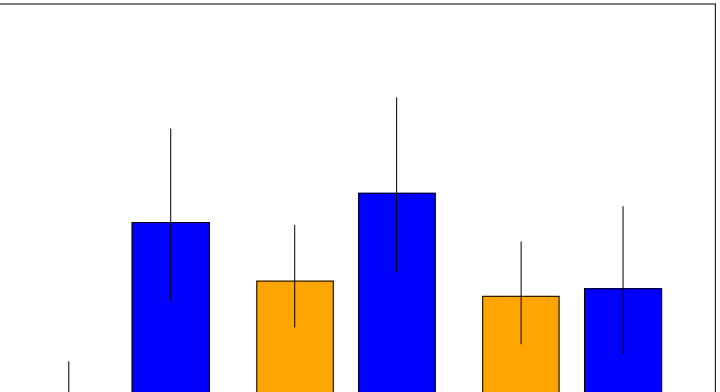
n 5-17 months of age at enrollment - clinical malaria



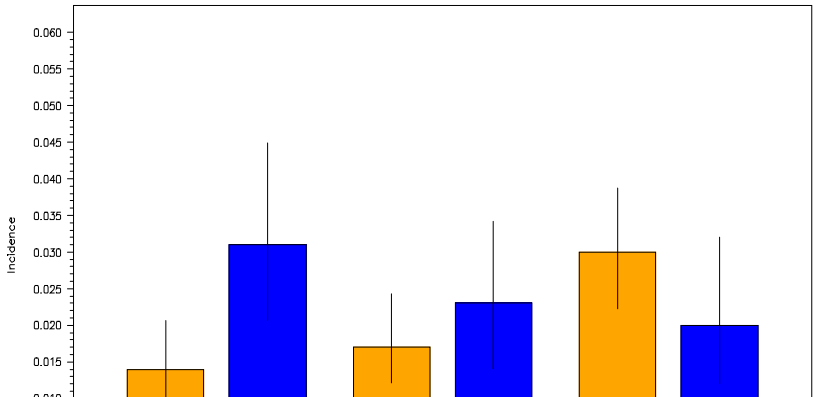
B. Infants 6-12 weeks of age at enrollment - clinical malaria



n 5-17 months of age at enrollment - severe malaria



D. Infants 6-12 weeks of age at enrollment - severe malaria



O recommends Large scale Pilot plementation of RTSS in Africa

O recommends the pilot implementations of the 4-dose edule of the RTS,S/AS01 vaccine in 3–5 distinct emiological settings in sub-Saharan Africa, at national level, covering moderate-to-high transmission ings," with three doses administered to children ween 5 and 9 months of age, followed by a fourth dose 18 months later.

s to involve sufficiently large populations also to ess,

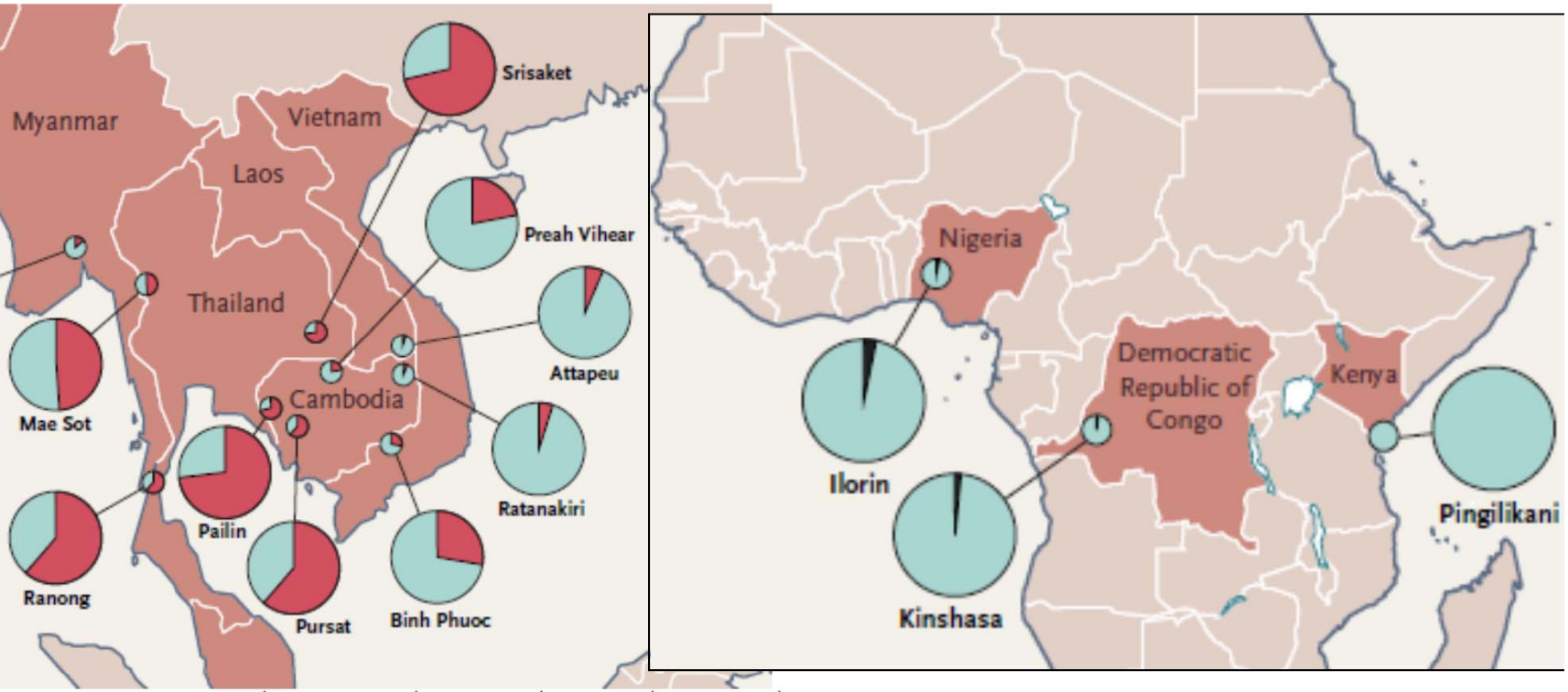
easibility of providing all four doses of RTS,S to the target ge group through existing health services;

mpact of RTS,S on child mortality;

vidence of any causal relationship between RTS,S and either neningitis or cerebral malaria, in the context of surveillance of dverse events; as well as the compilation of evidence on the

Applications for Tackling Challenges in Control and Elimination

curance of Artemisinin Resistance



artemisinin resistance		containment activities started	AL		AS-MQ		DHA-PPQ	
suspected year of emergence	detected		D3+	TF	D3+	TF	D3+	TF
2001*	2006	2009	♦	♦	♦	♦	♦	♦
2013	2013	2014	♦	-				
2001*	2008	2011	♦	-	♦	-	♦	-
2001*	2008	2009	♦	♦	♦	♦		

Parasite clearance half-life ≤5 hr

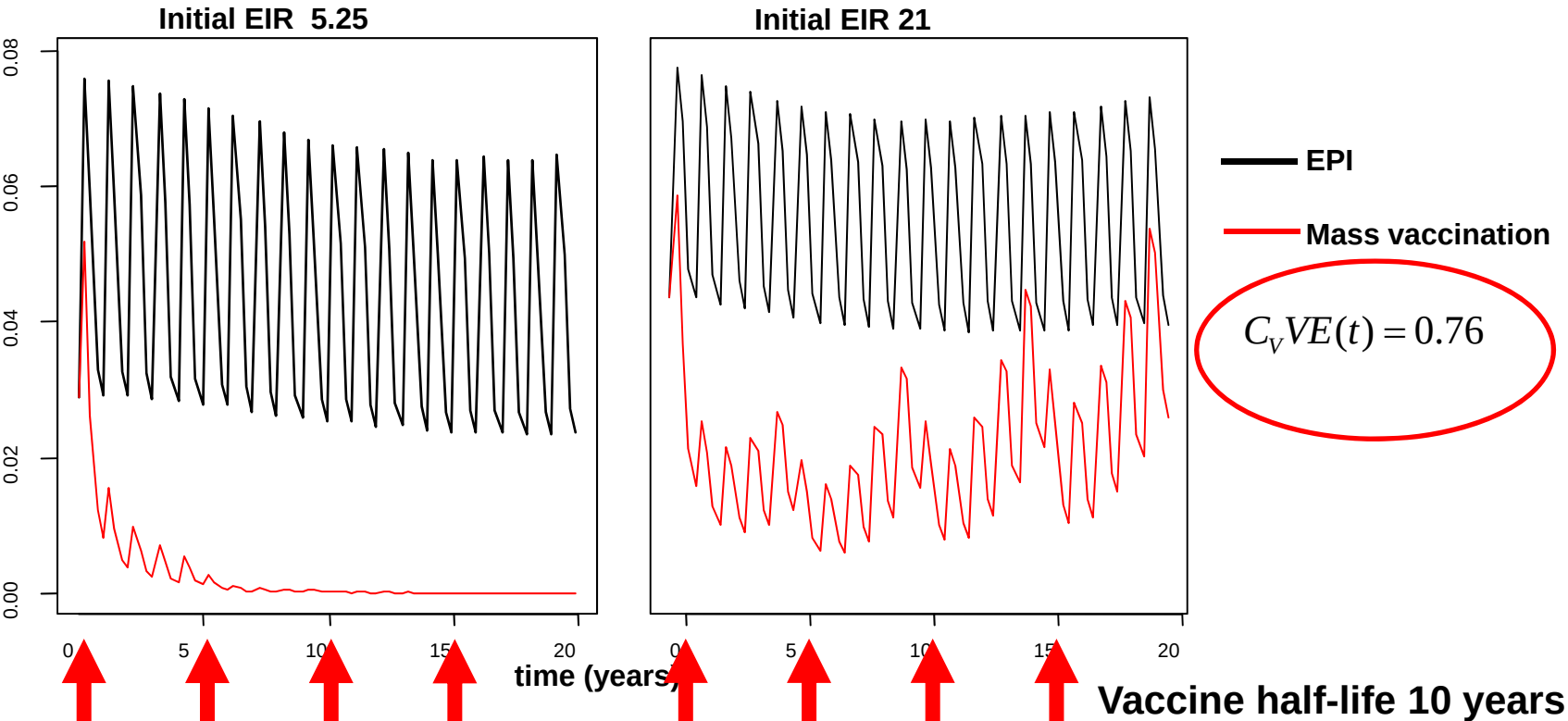
Parasite clearance half-life >5 hr, *kelch13* polymorphisms at or beyond amino acid position 441

Parasite clearance half-life >5 hr, no *kelch13* polymorphisms at or beyond amino acid position 441

odel predictions of Pre-Erythrocytic Vaccine effects over time

nterruption of transmission for initially low EIR

ettings with very high efficacy vaccines

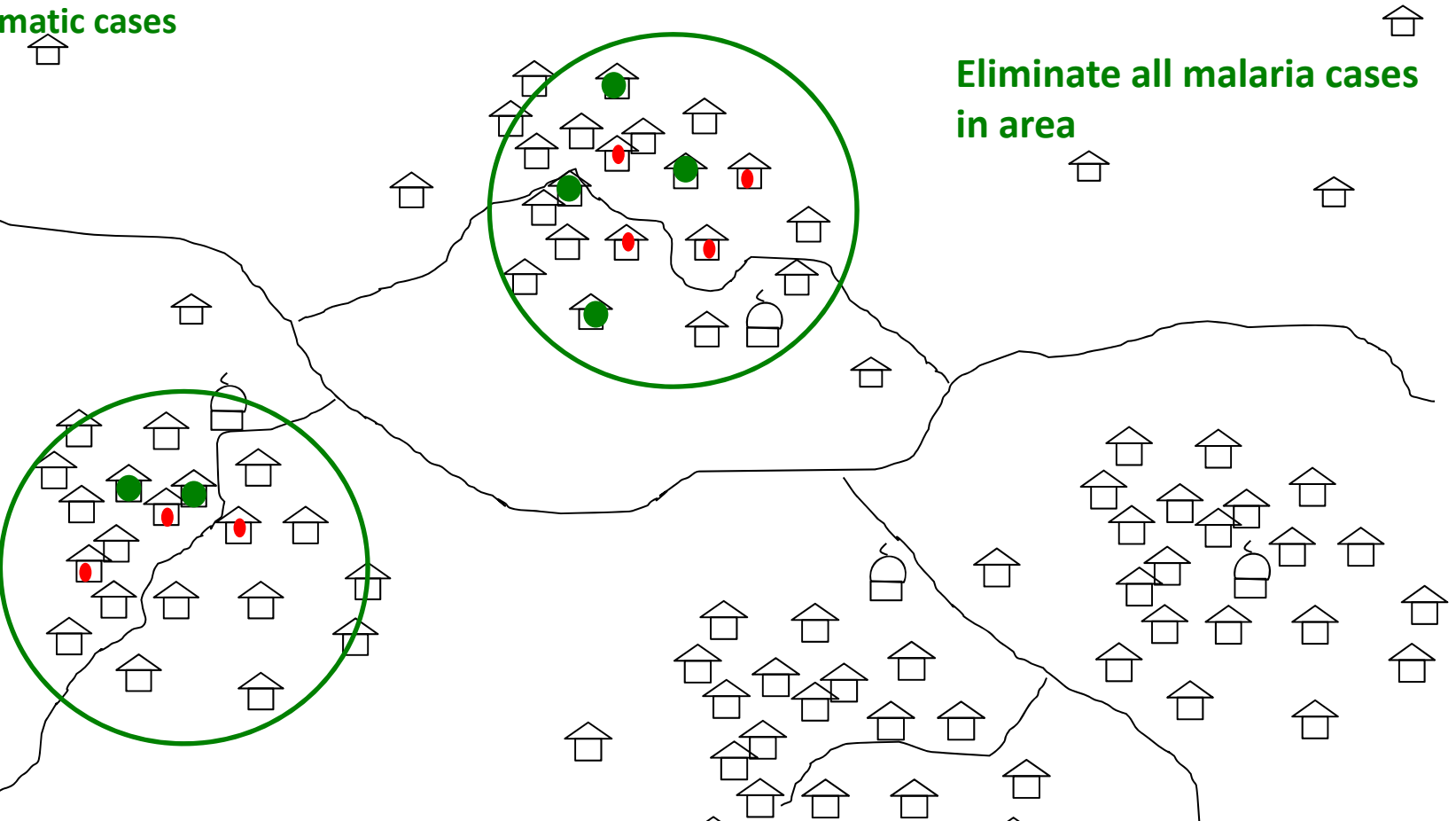


cations in Surveillance Response systems: screening and treatment (FSAT) in areas passively-detected foci

urrounding houses with very test (e.g. LAMP) to detect matic cases

Malaria cases presenting at health centres over a few months

Eliminate all malaria cases in area



me take home messages

- rrent malaria control and elimination tools do not ovide complete protection.
- rtially efficacious malaria vaccines are of benefits public health setting especially in high burden eas.
- ot implementation of first generation malaria ccine will provide insights in the best approach for ge scale deployments
- ploration of use of vaccines also to address nerging challenges (drug and insecticide sistance and responses to hot spots) to control d elimination need to be implemented.
- alaria Vaccines are an essential part of integrated