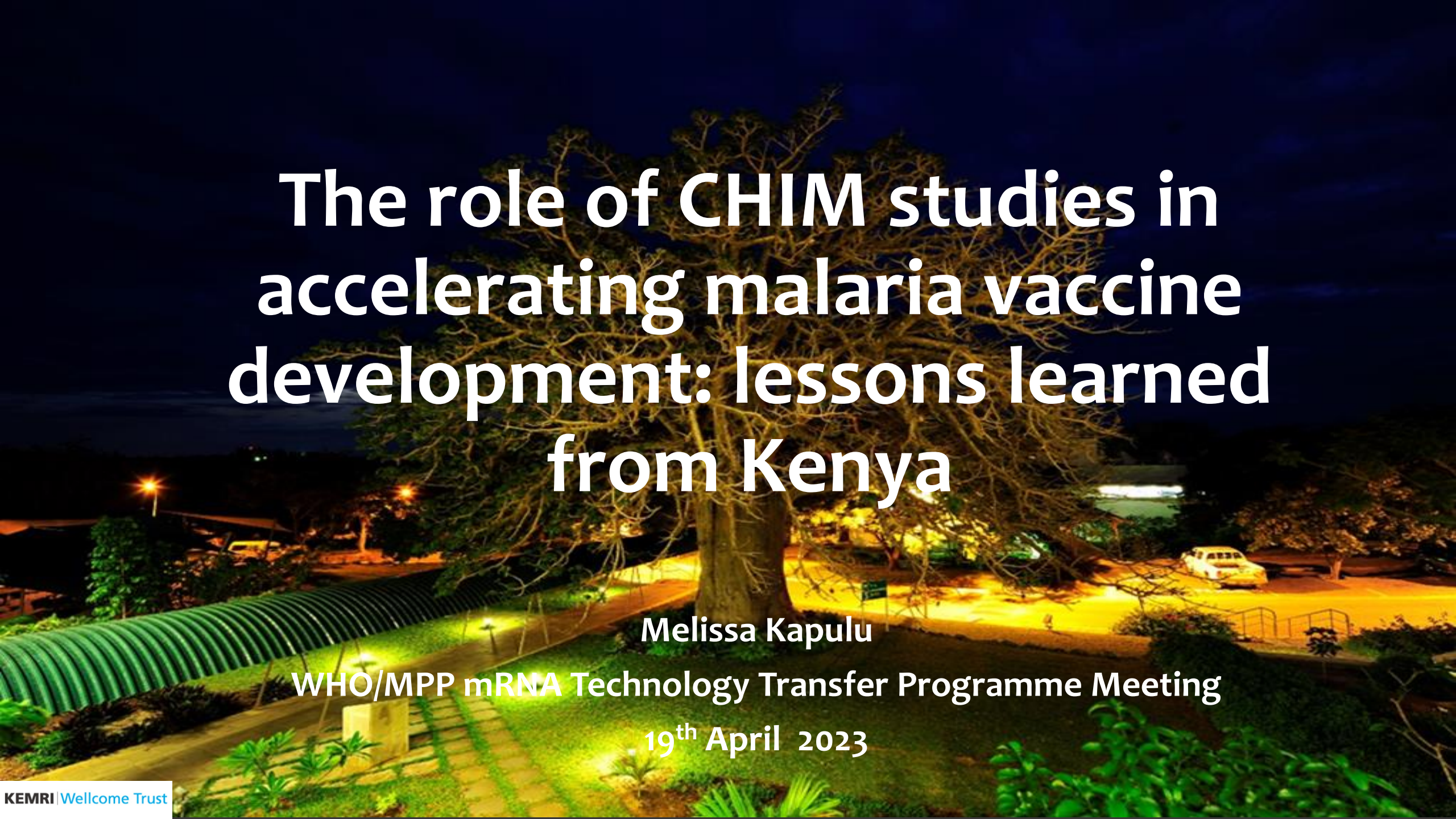

The role of CHIM studies in accelerating malaria vaccine development: lessons learned from Kenya

Melissa Kapulu

WHO/MPP mRNA Technology Transfer Programme Meeting

19th April 2023

KEMRI | Wellcome Trust

KEMRI-Wellcome Trust Research Programme

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Human Infection Studies

"Human infection studies (also known as human challenge trials and controlled human infection models) have the power to rapidly accelerate the development of much-needed vaccines and treatments……"

https://wellcome.org/news/what-are-human-infection-studies-and-why-do-we-need-them-covid-19

CHMI in Africa

<100
Vaccine efficacy
TBM
IBSM

<50
Infectivity

>100
Vaccine efficacy

>100
Vaccine efficacy
Infectivity

Purified cryopreserved sporozoites – PfSPZ Challenge

SANARIA
MALARIA ERADICATION THROUGH VACCINATION

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TBM: Transmission-blocking model
IBSM: Induced blood-stage model

>200
Infectivity
Vaccine efficacy
TBM
IBSM

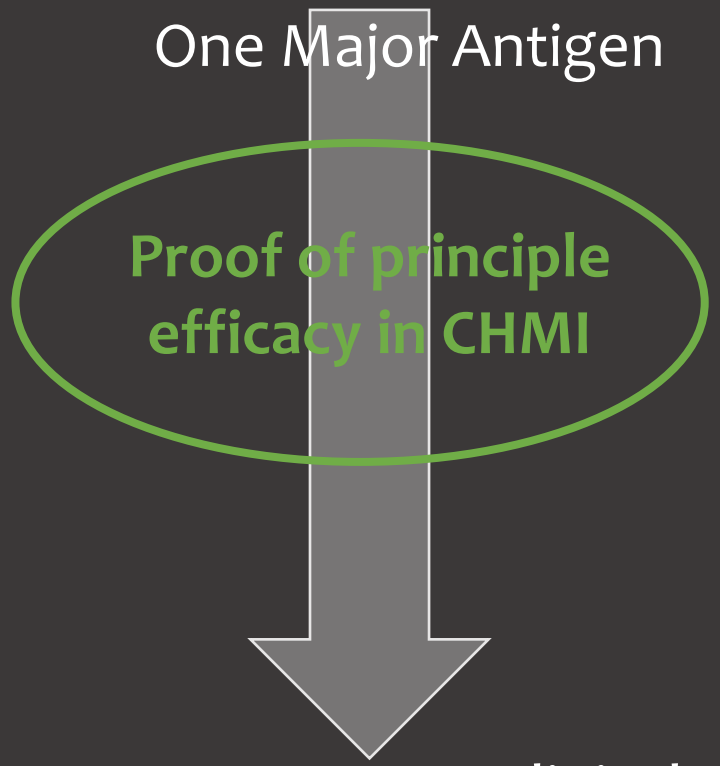
>100
Infectivity
Vaccine efficacy
TBM
IBSM

Modified from Kibwana, Kapulu, Bejon 2022

Role of CHMI in Malaria Vaccine Development

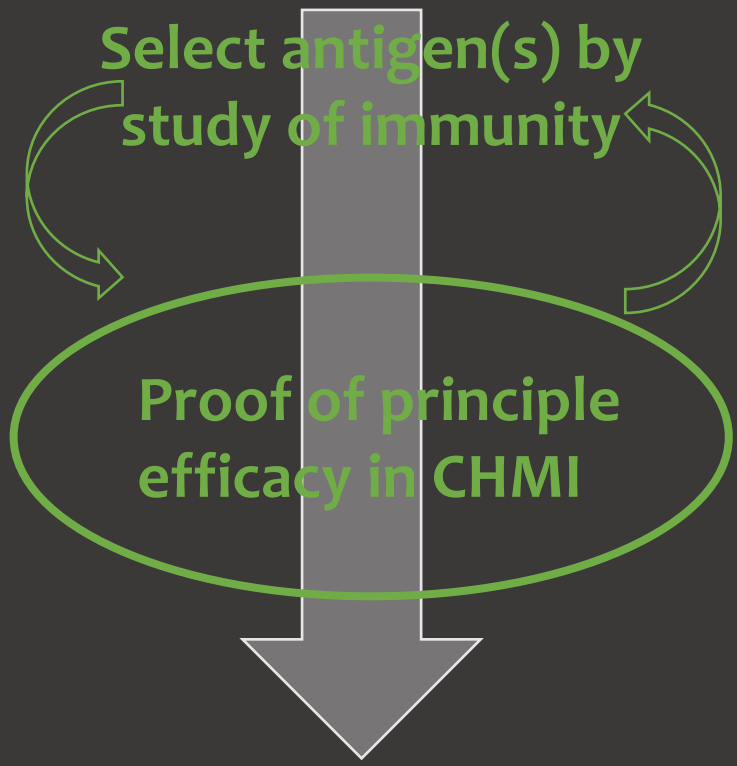
Anti-Infection stage

One Major Antigen



Progress onto clinical trials in target population
100s of children

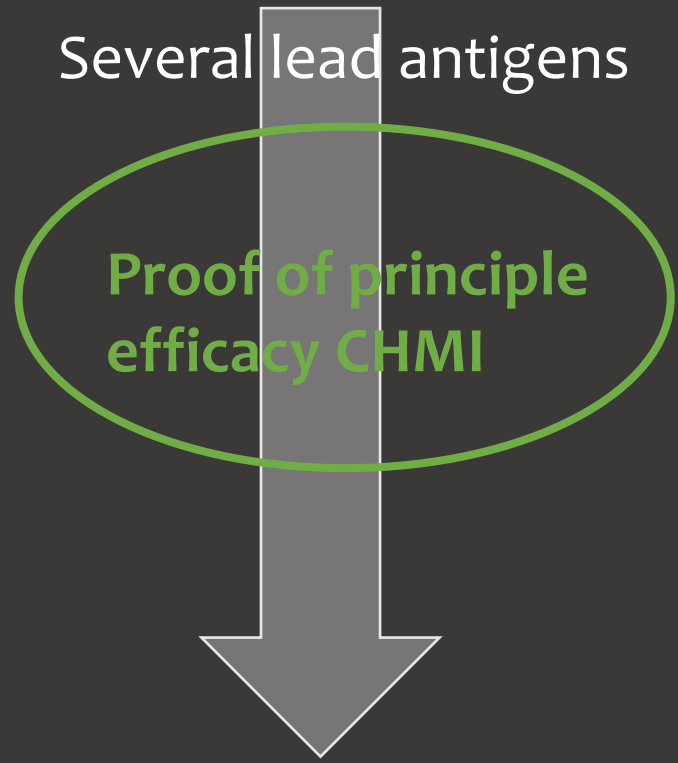
Anti-Disease stage



Progress onto clinical trials in target population
100s of children

Anti-Transmission stage

Several lead antigens



Progress onto clinical trials in target population
100,000s of people

Rationale for Malaria Challenge Studies in Semi-Immune Adults?

- [Better] Understand Naturally Acquired Immunity
  - ✓ Correlates (surrogate markers) of immunity/infection
- Accelerate Vaccine Development
  - ✓ Target antigen discovery and development
- Test Efficacy of Vaccines (and/or drugs/treatments)
  - ✓ Correlates (surrogate markers) of protection

Controlled Human Malaria Infection Platform

Study	Study of Immunity	Vaccine Efficacy	Transmission Model	Blood-stage Model	Vivax (led by MORU, Thailand)
Funder	Wellcome	EDCTP	Wellcome	MRC UKRI	Wellcome
No. of Volunteers	161	80	104	60	126
Aim	Vaccine Antigen Discovery	Test Vaccines	Test Blocking of Mosquito Infectivity	Test Sterile Immunity to Blood-Stages	Vaccine Antigen Discovery
Status	Completed (2021)	Ongoing	Ongoing	Planned	Ongoing

Plasmodium falciparum

Plasmodium vivax

Embedded Social science and empirical ethics research across all studies

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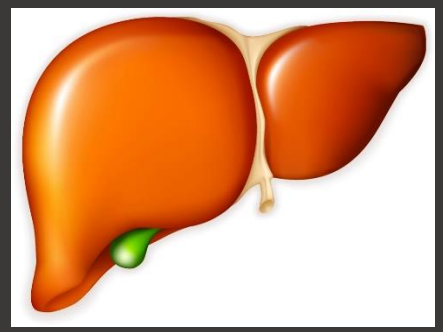
Controlled Human Malaria Infection in Our Setting

Day 0: Inject Sporozoites

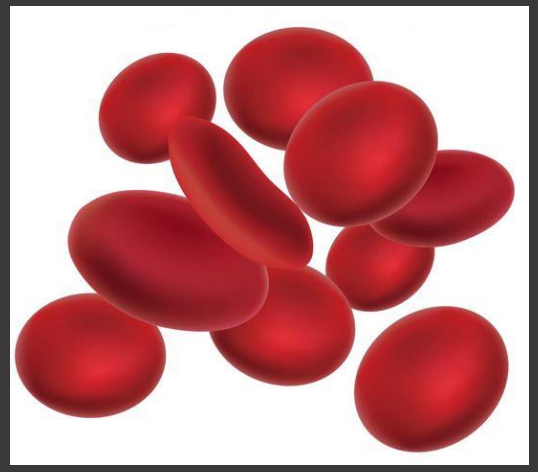
Day 0-6: Liver Incubation



Days 7 onwards: parasites multiply in blood, opposed by immunity

Use Daily **qPCR** to quantify parasites

Follow up for 21 days and endpoint treatment with Artemether Lumefantrine (3 day observed)



*Sickle cell trait an exclusion criteria

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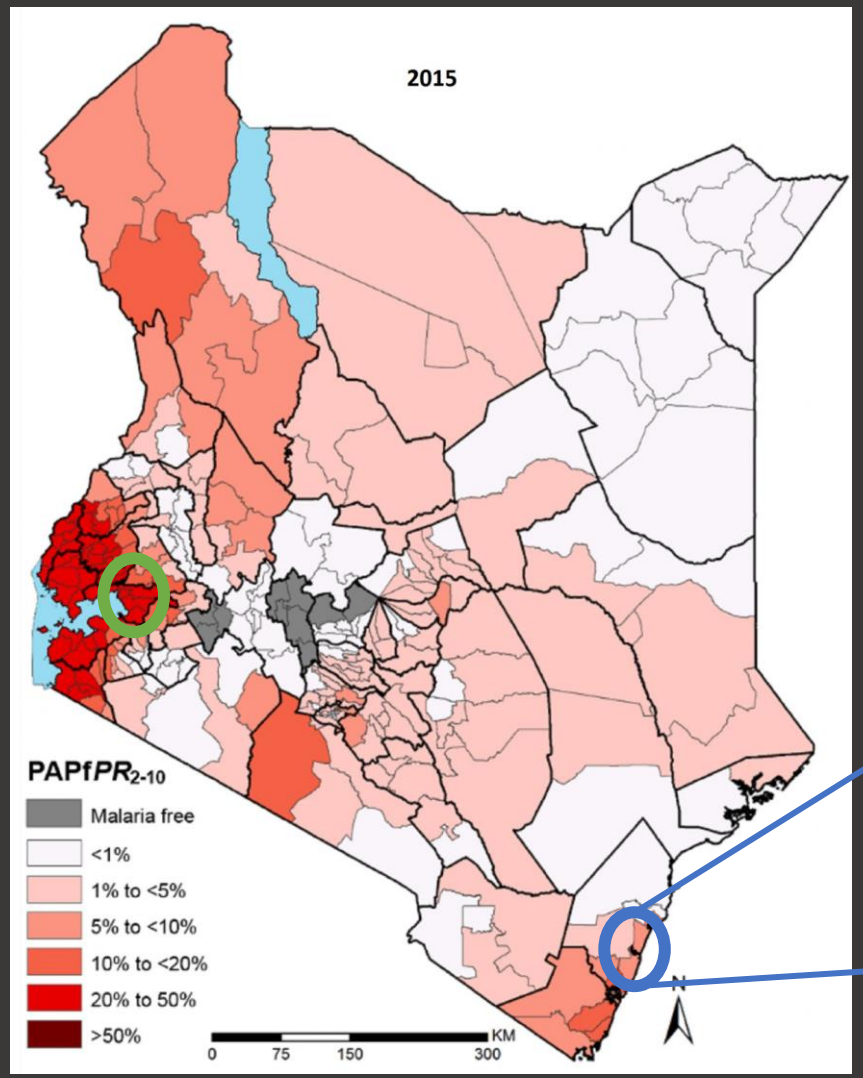
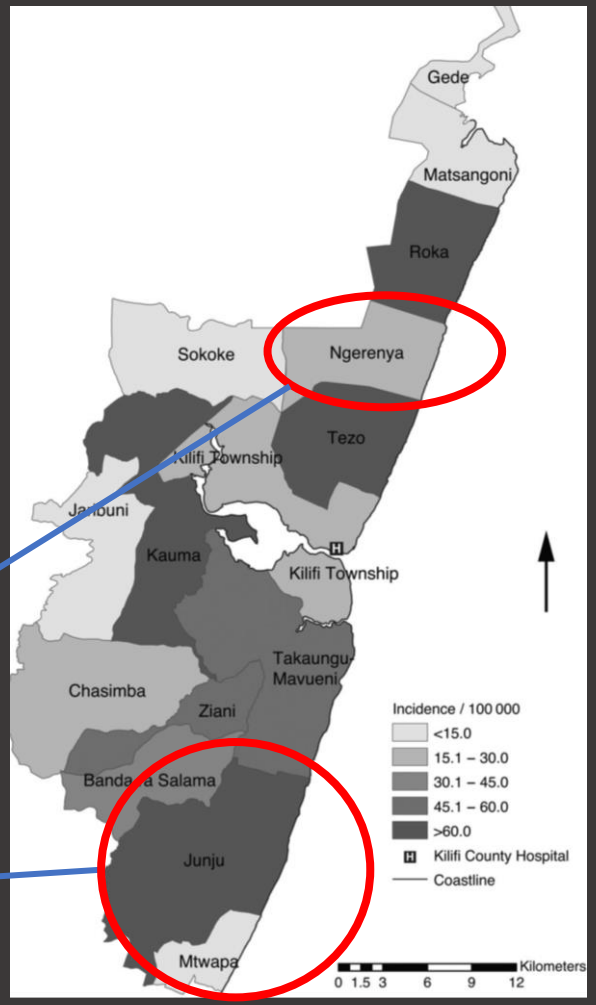
Study of Immunity in CHMI

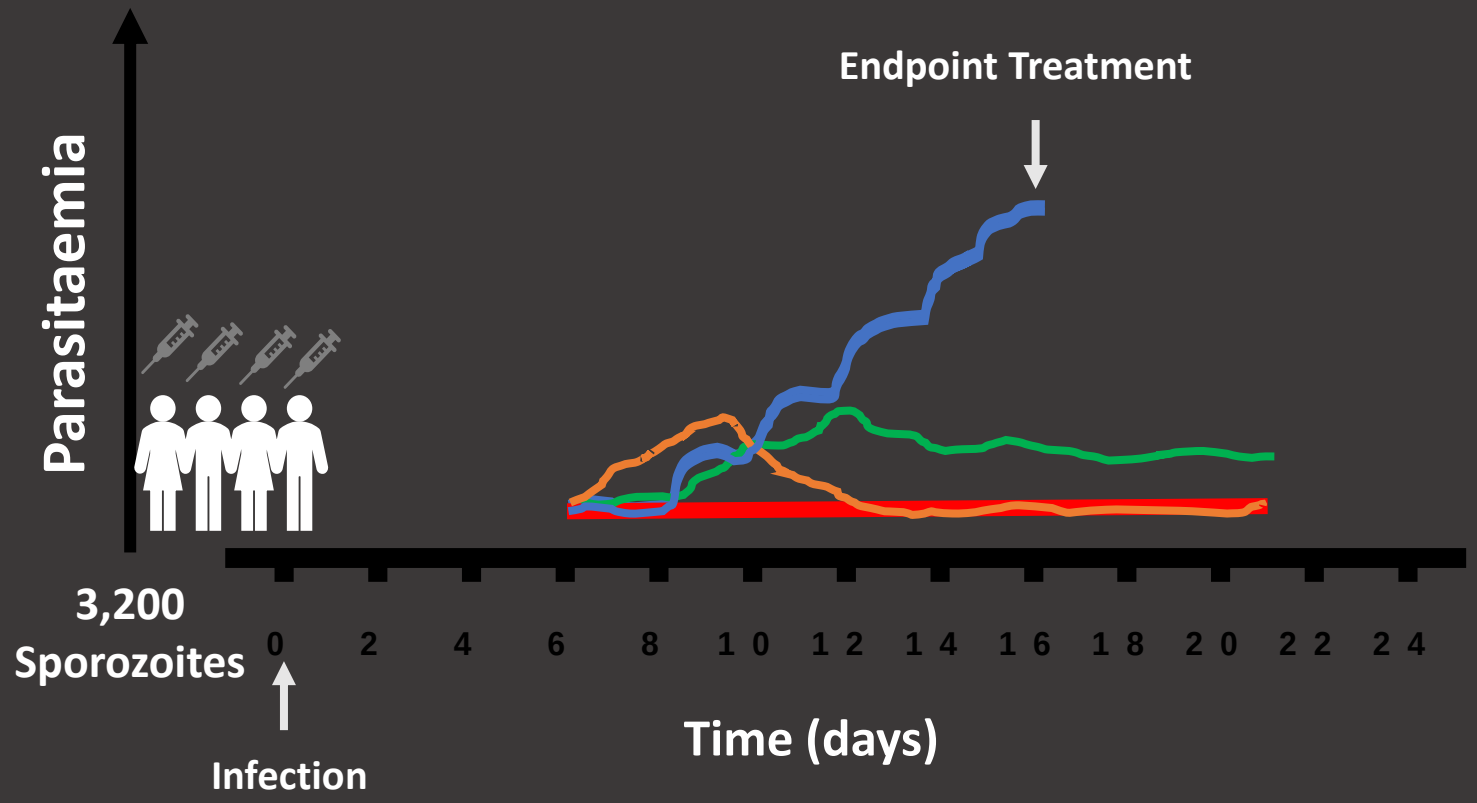




- Healthy semi-immune adults with varying degrees of immunity (screened for range of natural exposure) from:
  - ✓ Ahero – moderate-high exposure
  - ✓ Kilifi South – moderate exposure
  - ✓ Kilifi North – low to no exposure

Adapted from Kapulu et al 2019

Key Outcome following CHMI



Highly immune Phenotype

Clearance Phenotype

Slow Growth Phenotype

Susceptible Phenotype

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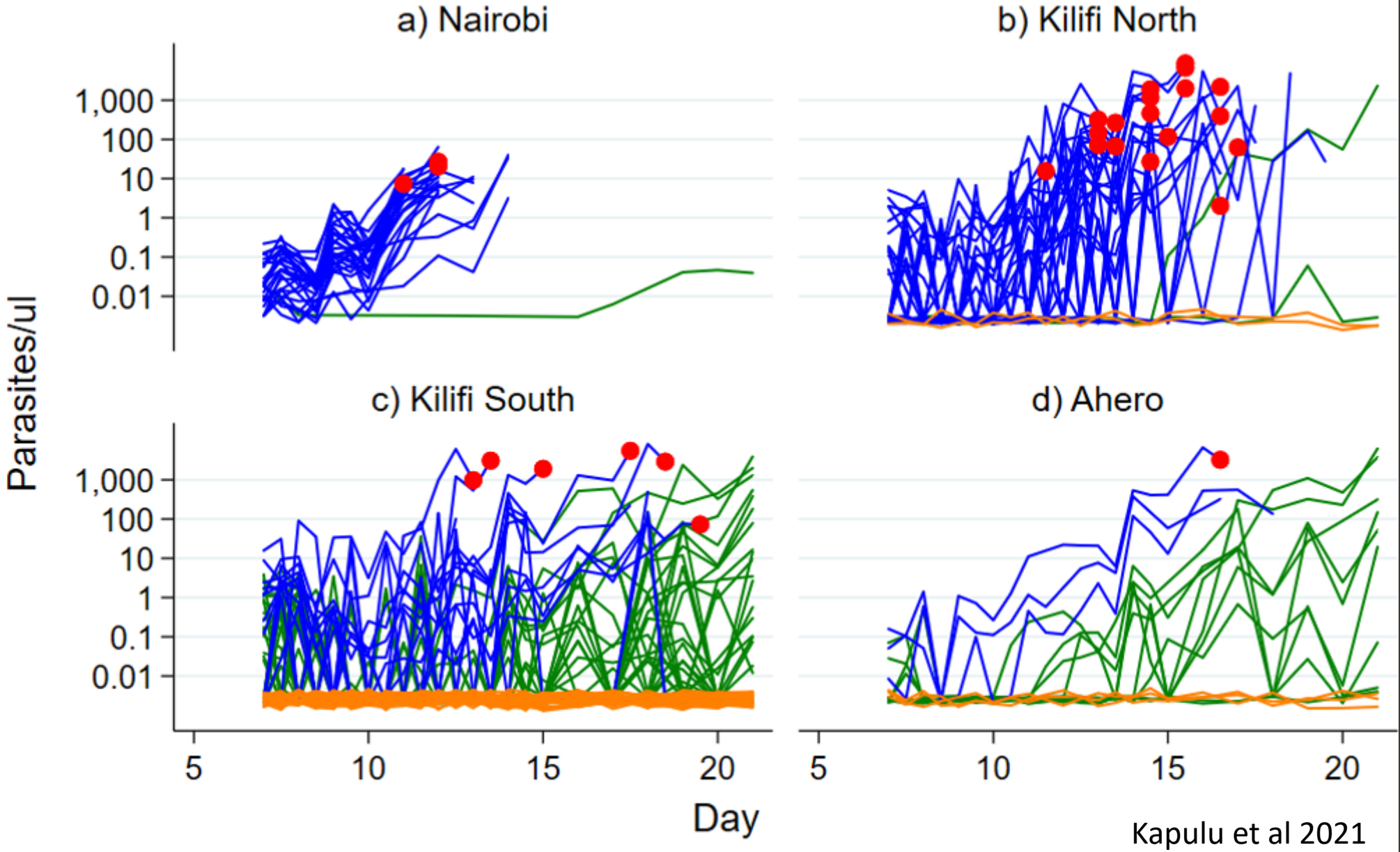
Parasite growth following CHMI

Parasites Detected and Treatment Needed

Febrile Episode

Parasites Detected but no Treatment Needed

No Parasites Detected



Kapulu et al 2021

Multi-stage Vaccine Efficacy in CHMI

Recruitment from Kilifi North – low exposure population

Week	0	4	8	12
R21 (ID) N=24	R21/ Matrix M 10µg /50µg	R21/ Matrix M 10µg /50µg	R21/ Matrix M 10µg /50µg	CHMI (ID)
ME-TRAP (ID) N=24	ChAd63 ME-TRAP $5x10^{10}$ vp		MVA ME-TRAP $2x10^{8}$ pfu	CHMI (ID)
R21 (IV) N=14	R21/ Matrix M 10µg /50µg	R21/ Matrix M 10µg /50µg	R21/ Matrix M 10µg /50µg	CHMI (DVI)
Control (ID) N=18				CHMI (ID)

ClinicalTrials.gov Identifier: NCT03947190

This project is part of the EDCTP2 programme supported by the European Union

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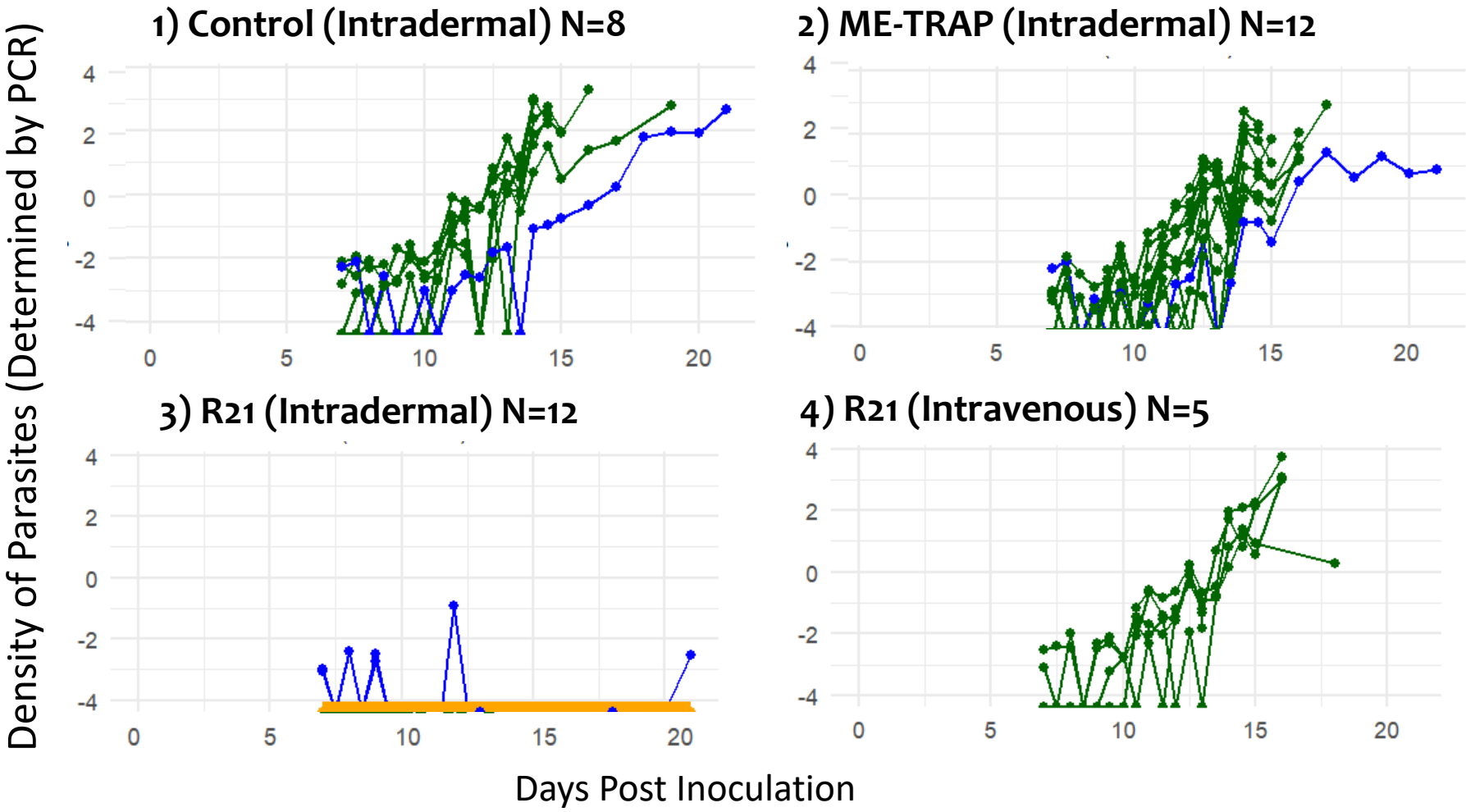
THE JENNER INSTITUTE
DEVELOPING INNOVATIVE VACCINES

EDCTP

MMVC Multi-Stage Malaria Vaccine Consortium

Testing Efficacy of Vaccines: Parasite Growth



- ✓ R21: High efficacy
- ✓ ME-TRAP: Down select

Key Outcomes for Vaccine Efficacy Study

Parasites Detected by PCR	Threshold for Treatment Reached	Control (ID) n=8	ME-TRAP (ID) N=12	R21 (ID) n=12	R21 (DVI) n=5
No	No	0 (0%)	0 (0%)	9 (75%)	0 (0%)
Yes	No	**1 (12.5%)**	1 (8.3%)	3 (25.0%)	0 (0%)
Yes	Yes	7 (87.5%)	11 (91.7%)	0 (0%)	5 (100%)

- ❖ Demonstration of in vivo mechanisms of protection
- ✓ R21-induced immunity protects against ID challenge and avoided by IV route
- ✓ Synergy between R21-induced and anti-blood stage immunity: i.e., parasites that breakthrough R21-induced immunity mopped up by anti-blood-stage immunity

Summary

- Community considerations & consultations in design, introduction, and implementation
- Early engagement of Ethics & Regulatory Authorities
- CHIM model powerful tool for translational & discovery research
  - ✓ Rapid down selection of vaccines
  - ✓ Antigen discovery and vaccine development
  - ✓ Disease and immune mechanisms
  - ✓ Cultural and societal behaviour

Guidelines to include Challenge Studies in Kenya (first issued January 2020)

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