



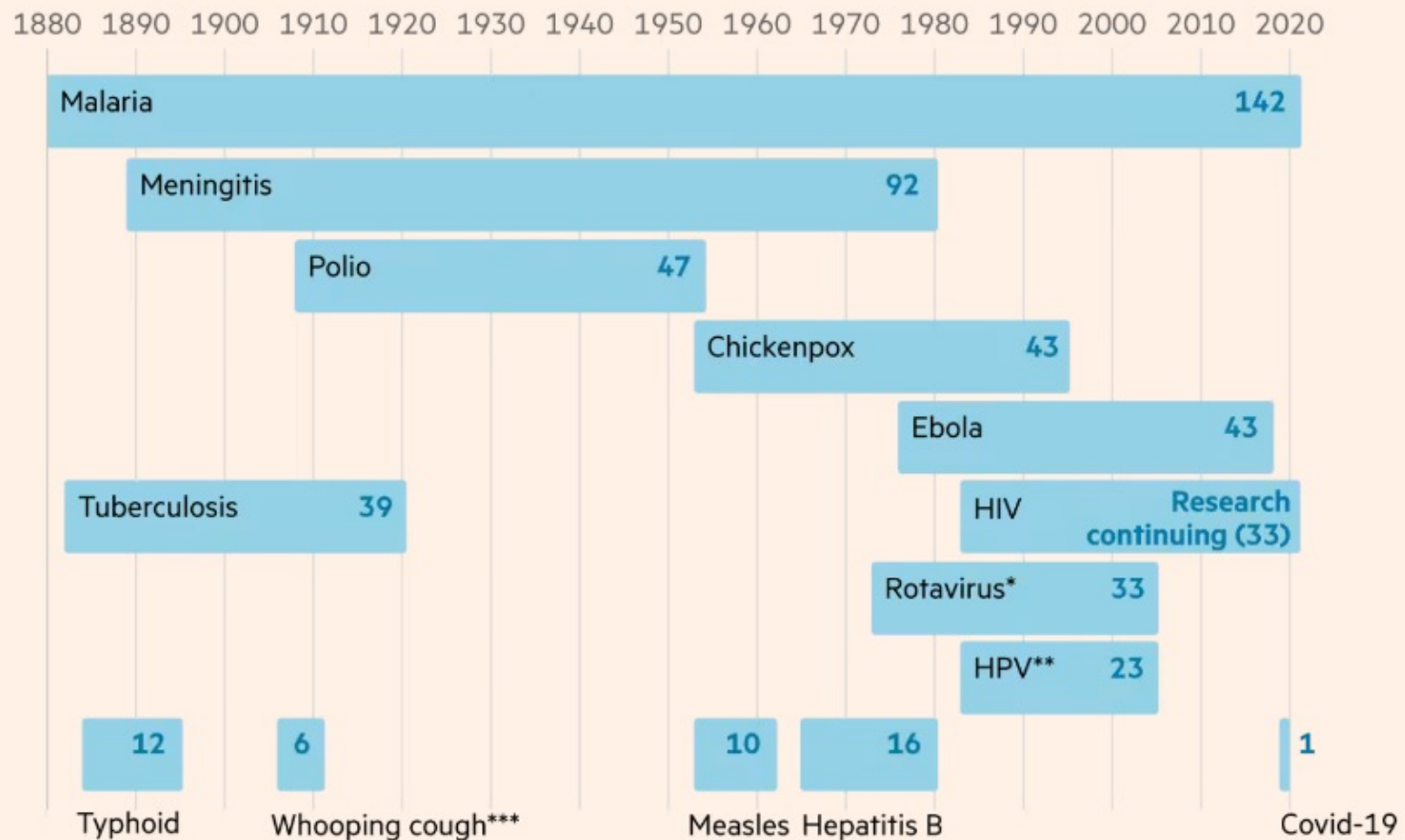
Academic Vaccine Development for Malaria

Professor Sir Adrian V. S. Hill

**The Jenner Institute
University of Oxford**

Vaccine innovation : Time from Pathogen Discovery to a Deployed Vaccine

Time taken to develop vaccine from discovery of infectious agent, in **years**



*Diarrhoeal disease **Cervical cancer ***Pertussis

Sources: FT research; OurWorldinData



Malaria: The Problem

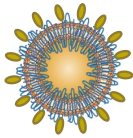
- About 500,000 deaths each year
- Mainly of young children
- Over 90% of deaths in Africa
- About \$500 million dollars a year spent “controlling” malaria
- Vaccines rolled out for the first time in 2024



Malaria Vaccines

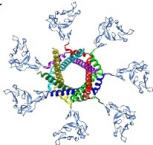
Can Target Three Life-Cycle Stages

1. Sporozoite Stage

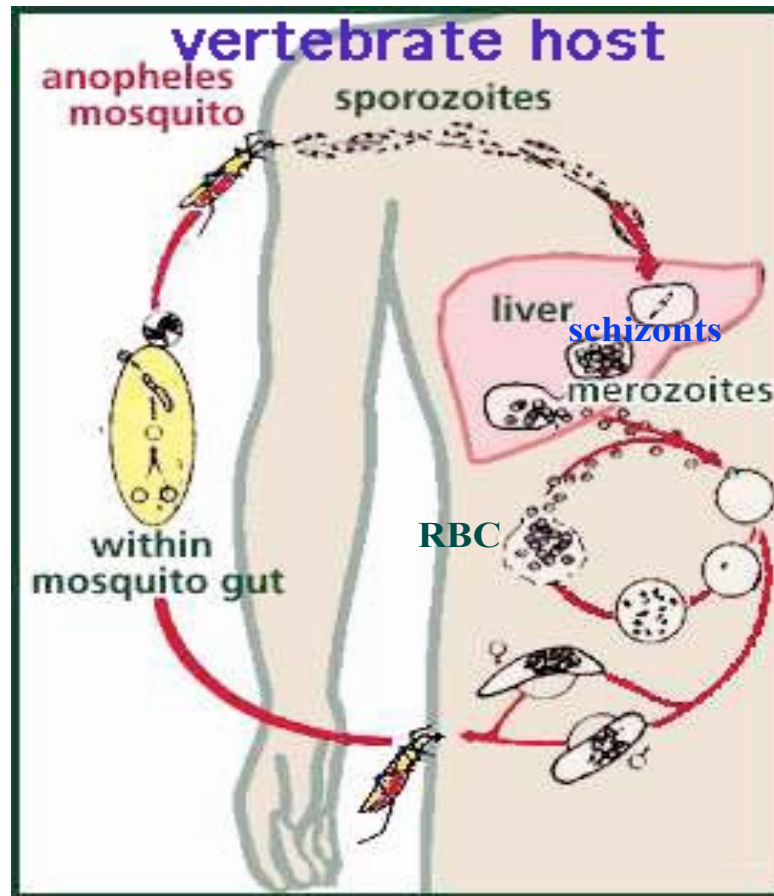


R21 nanoparticle

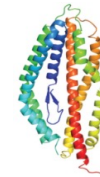
3. Mosquito Stage



Pfs48/45



2. Blood Stage



PfRH5



Over 115 Years of Malaria Vaccine Research



Edmond & Etienne Sargent

Les Comptes Rendu de l'Academie des Sciences 151: 407-409, **1910**

Immunity in avian malaria: maintenance *in vitro* of *Plasmodium relictum* sporozoites. Partial immunity by inoculation of sporozoites

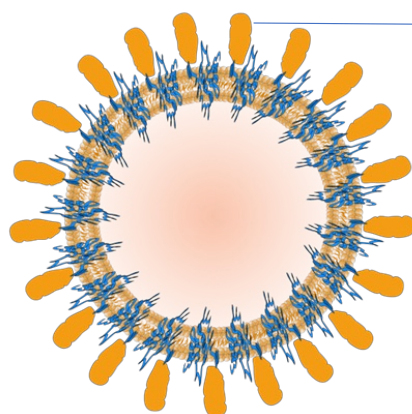
150 different malaria vaccine candidates have entered clinical trials since then

R21/Matrix-M™ Malaria Vaccine

R21 - Oxford
(from 2011)

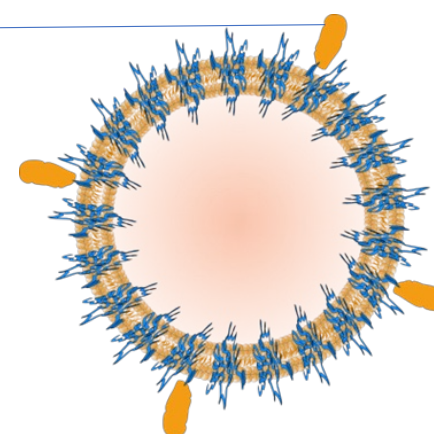
RTS,S - GSK
(from 1984)

Lower dose
Lower cost
Higher efficacy
& immunogenicity
Better durability
20-fold more supply



5µg

CS Proteins



25µg

plus 50µg **Matrix-M™**
saponin adjuvant



plus 50µg **AS01™**
saponin adjuvant

- R21 consists of the central repeat and C-terminus of the CS protein fused to the N-terminus of the HBsAg.
- RTS,S required expression of a four-fold excess of the unfused HBsAg to allow it to form hybrid particles.

Source: Collins KA, et al. Enhancing protective immunity to malaria with a highly immunogenic virus-like particle vaccine. Scientific reports. 2017;7:46621





Vac076

a Phase IIb Safety, Immunogenicity and Efficacy Trial in 5 – 17 Month Olds at Nanoro, Burkina Faso

Week	0	4	8
Group 1 N = 150	5µg R21 / 25µg Matrix-M	5µg R21 / 25µg Matrix-M	5µg R21 / 25µg Matrix-M
Group 2 N = 150	5µg R21 / 50µg Matrix-M	5µg R21 / 50µg Matrix-M	5µg R21 / 50µg Matrix-M
Group 3 N = 150	Control vaccine	Control vaccine	Control vaccine

Vaccinations started May – July 2019

Interim analysis Q3 2020; Q3 2021

Booster dose of R21/MM in June 2020, 2021, 2022

Follow-up of all subjects to 2023

PI: Halidou Tinto; Funding: EDCTP



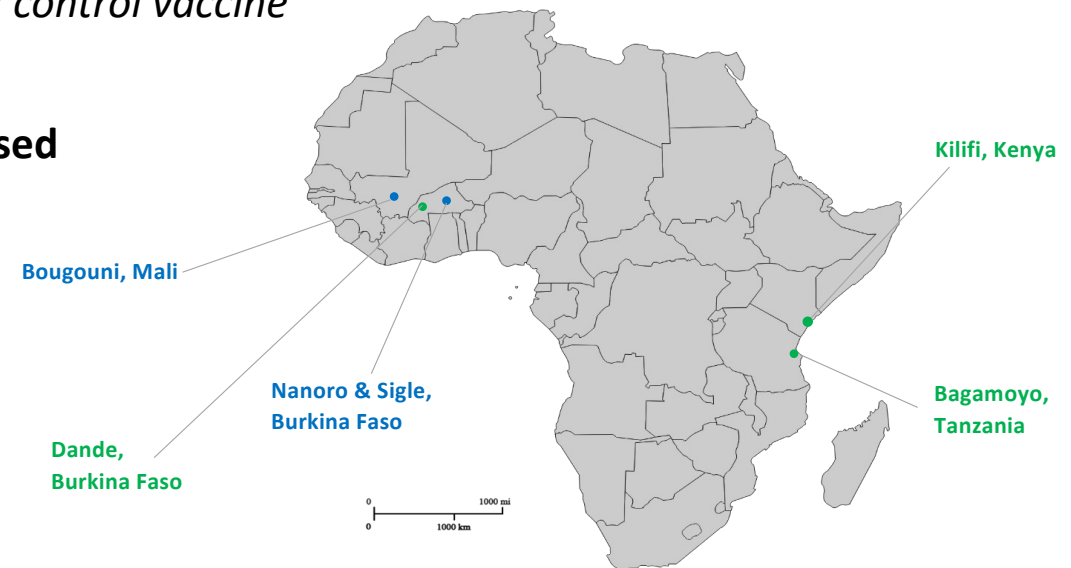
Phase III Trial Design

- **Participants:** 4800, age **5-36** months at enrolment
- **Randomisation:** **2:1** – *5µg R21/50µg Matrix-M™ : control vaccine*
- **Double-blind**
- **Seasonal** and **standard** vaccination regime assessed

	Month 0	Month 1	Month 2	Boost (Month 14)
Group 1 n = 3200	5µg R21/ 50µg Matrix-M™	5µg R21/ 50µg Matrix-M™	5µg R21/ 50µg Matrix-M™	5µg R21/ 50µg Matrix-M™
Group 2 n = 1600	Control vaccine	Control vaccine	Control vaccine	Control vaccine



Mehreen Datto, Jenner- Oxford



**Ally
Olotu**



**Alassane
Dicko**



**Jean-Bosco
Ouédraogo**



**Mainga
Hamaluba**



**Halidou
Tinto**

Vaccine Efficacy in 5–17-month-old Vaccinees by Site

for time to first episode over one year, mPP analysis

		R21 group				Control group				
	Study Site	N	n	T	n/T	N	n	T	n/T	Adjusted VE** (95%CI)
M2.5– M14^	Seasonal	751	110	645.0	0.17	382	179	227.7	0.79	0.79 (0.73, 0.83)
	Standard	673	48	620.2	0.08	346	88	294.2	0.30	0.75 (0.65, 0.83)
	Nanoro	382	93	309.7	0.30	193	125	87.6	1.43	0.76 (0.69, 0.82)
	Bougouni	369	17	335.3	0.05	189	54	140.1	0.39	0.86 (0.76, 0.92)
	Dande	308	22	288.5	0.08	160	57	130.3	0.44	0.83 (0.72, 0.90)
	East African	365	26	331.7	0.08	186	31	163.9	0.19	0.60 (0.32, 0.76)

Very High Efficacy of 79% and 75% at seasonal and standard sites in year 1 in 5-17 month olds

Malaria Vaccine Distribution in 2024

**R21/MM for Chad, DRC, Mozambique, South Sudan,
Central African Republic, Nigeria, Ivory Coast,
Uganda, Ghana, Burkina Faso**

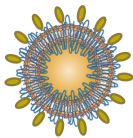
RTS,S/AS01 for Ghana, Kenya, Malawi, Benin, Burkina
Faso, Burundi, Cameroon, DRC, Liberia, Uganda, Niger,
& Sierra Leone



Malaria Elimination Vaccines

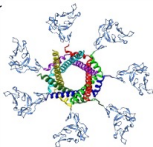
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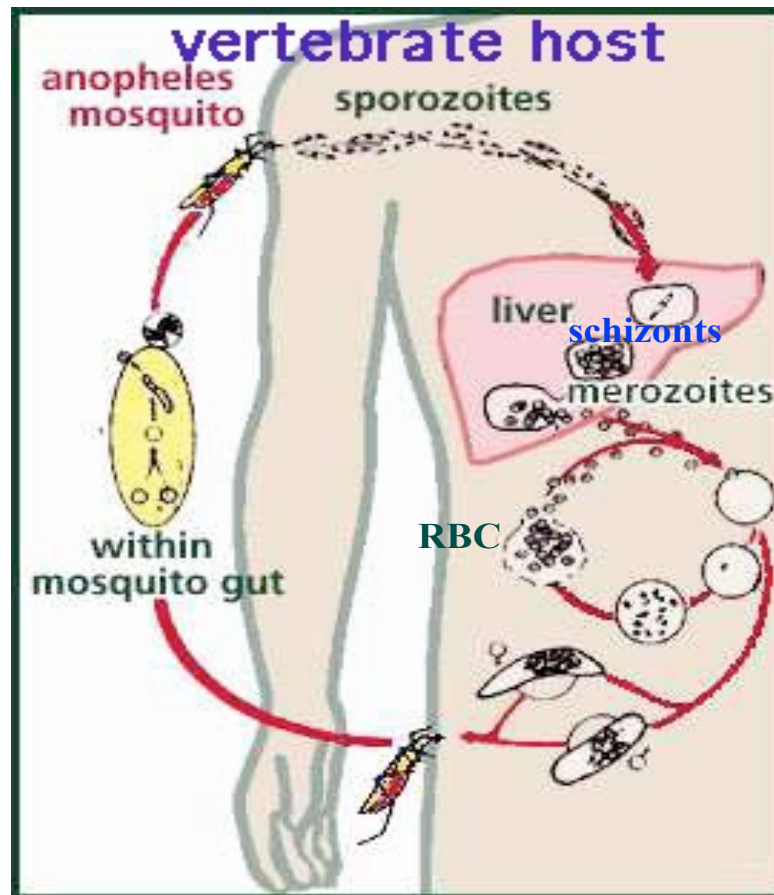


R21 nanoparticle

3. Mosquito Stage



Pfs230
and/or Pfs48/45



2. Blood Stage

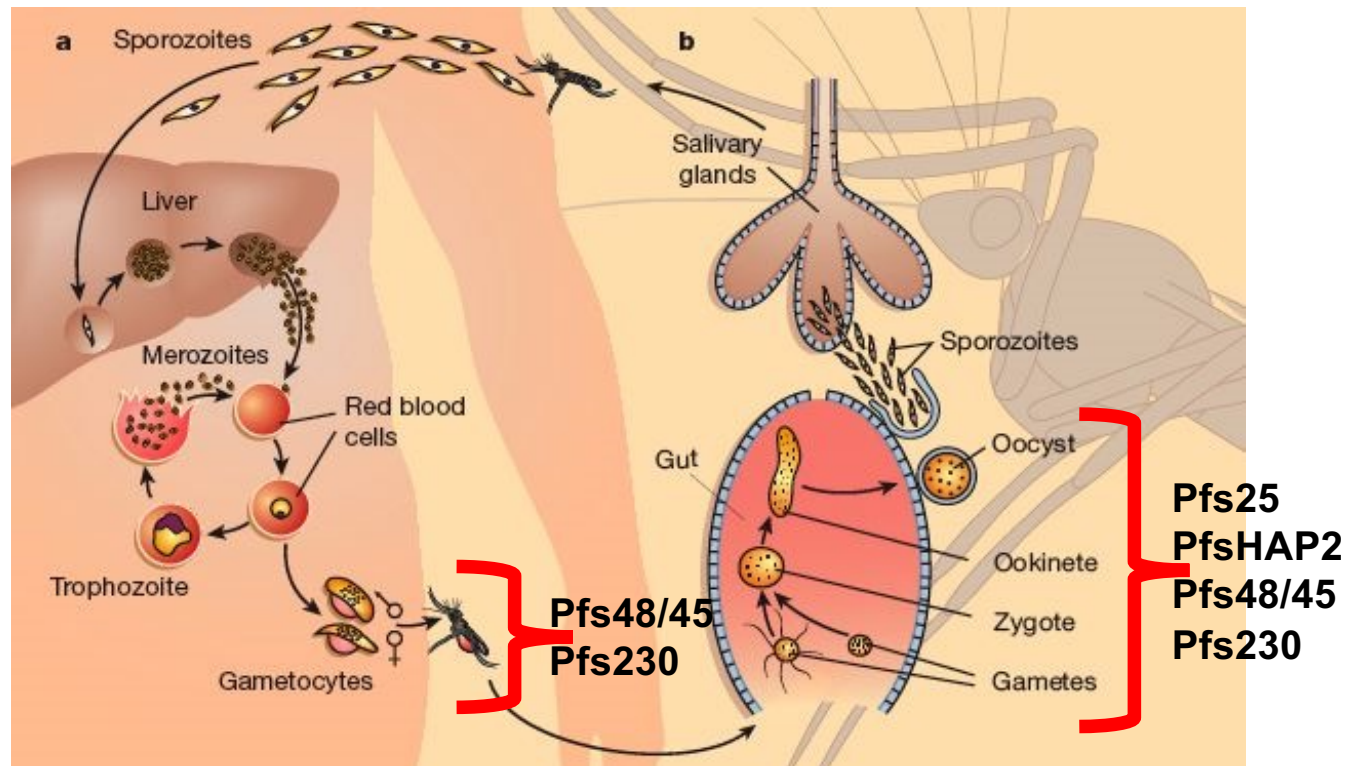


PfRH5



Transmission Blocking Vaccines

Parasite Candidate Antigens



a: Expressed in host

b: Expressed in vector



Three-Stage Combination Malaria Vaccine

- R21/Matrix-M – licensed and being rolled out from 2024
- RH5.1 in Matrix-M* (MM)
 - 58% efficacy in Burkina Faso for RH5/MM – in phase IIB trials +/- R21/MM
 - Higher efficacy >75% against high-density parasitaemia cases
- Pfs230D1-CRM/MM – now entering phase Ib /II west African trials
and/or
- Pfs48/45/MM - Phase Ia completed; Burkina Faso trial ongoing

Serum Institute of India planning to provide a three-stage vaccine

*Simon Draper et al.

Bioko Island, Equatorial Guinea



Malabo



Potential 3-Stage Malaria Vaccine **Elimination** Trial

Starting with Bioko Island, Equatorial Guinea

300,000 population

MCD Global Health collaboration, Guillermo Garcia *et al.*

Announcement at UN headquarters on Wednesday...



New Analysis: Malaria Elimination to Boost African Economies by \$16 Billion Average Annually



Blog • News • Press Releases - 06/05/2024



June 5, 2024 (London) - The GDP of countries in Africa could rise by an additional \$126.9 billion if the UN target to cut malaria by 90% from 2015 levels by 2030 is met, according to research and analysis conducted by **Oxford Economics Africa**, in a new report entitled 'The Malaria Dividend' from **Malaria No More UK**.

This represents an average boost of nearly \$16 billion a year to ¹African economies, more than **10%** of collective annual spending on health for all countries in Africa.

\$127 billion benefit vs estimated \$15-20 billion cost of elimination!

¹<https://malarianomore.org.uk/sites/default/files/Zero%20Malaria%20-%20The%20Malaria%20Dividend%20ONLINE%20FINAL1.pdf>



Summary



- **Malaria Elimination is back on the Global Health agenda**
- **Two anti-sporozoite malaria vaccines are newly licensed**
 - a blood-stage vaccine should soon be added (RH5.1)
 - & also transmission-blocking vaccines
- **Initial elimination vaccine trials have started and others will follow**
 - New longer lasting anti-malarial drugs will complement vaccines in achieving elimination
- **An expensive goal – but succeed and the money is recovered many times over!**



African Clinical Trial Principal Investigators



- Ally Olotu, Ifakara Health Institute, Bagamoyo, Tanzania
- Alassane Dicko, Malaria Research and Training Center, Mali
- Jean-Bosco Ouedraogo, INSTech, Bobo-Dioulasso, Burkina Faso
- Mainga Hamaluba, KEMRI-Wellcome Unit, Kilifi, Kenya
- Halidou Tinto, Clinical Research Unit of Nanoro, Burkina Faso



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Malaria Vaccine Lead Investigators



Jenner Institute, Oxford team leads

- Mehreen Dattoo, lead clinician
- Lisa Stockdale & Katie Ewer, immunology
- Sophie Weston, project management
- Alison Lawrie, head of regulatory

Serum Institute of India team leads

- Umesh Shaligram, chief scientist
- Harish Rao, manufacturing
- Parag Nagarkar, regulatory
- Prasad Kulkarni, clinical



