OPTIMAL USE OF MALARIA VACCINES

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Annecy Dec 7th 2016

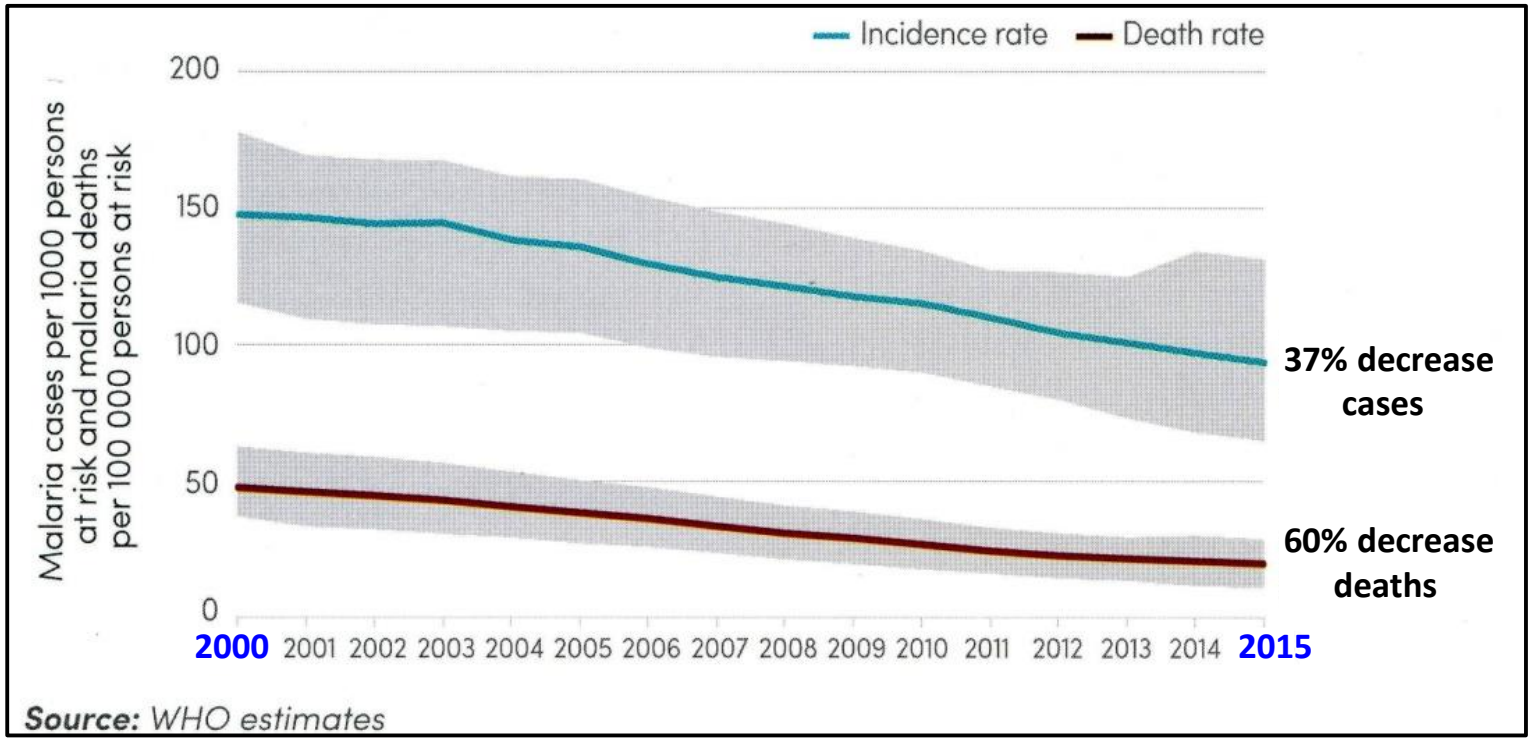
Improving health worldwide

www.lshtm.ac.uk

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

RECENT PROGRESS IN MALARIA CONTROL

Estimated numbers of clinical cases and malaria deaths



World Malaria Report 2015

BUT

438,000 [236 - 635,000] deaths/year

214 [149-303 million] cases/year

THE PERFECT MALARIA VACCINE

- A high level of efficacy (+/- 90%).
- Sustained protection.
- Effective against all strains of parasite (ideally against all species).
- A high safety record.
- A vaccination schedule compatible with routine immunisation schedules.
- Easy to produce at an affordable cost.

IMPLEMENTATION IN ALL AREAS WHERE MALARIA REMAINS A SIGNIFICANT CLINICAL PROBLEM

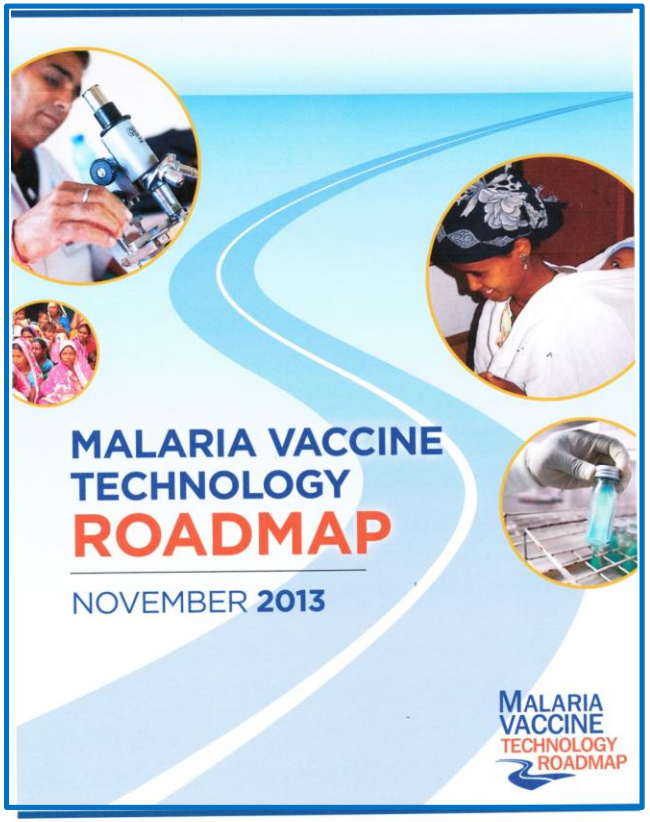
MALARIA VACCINE TECHNICAL ROADMAP

A more realistic objective

By 2030, license vaccines targeting *Plasmodium falciparum* and *Plasmodium vivax* that encompass the following two objectives:

- **Protective efficacy of at least 75 percent against clinical malaria suitable for administration to appropriate at-risk groups in malaria-endemic areas.**

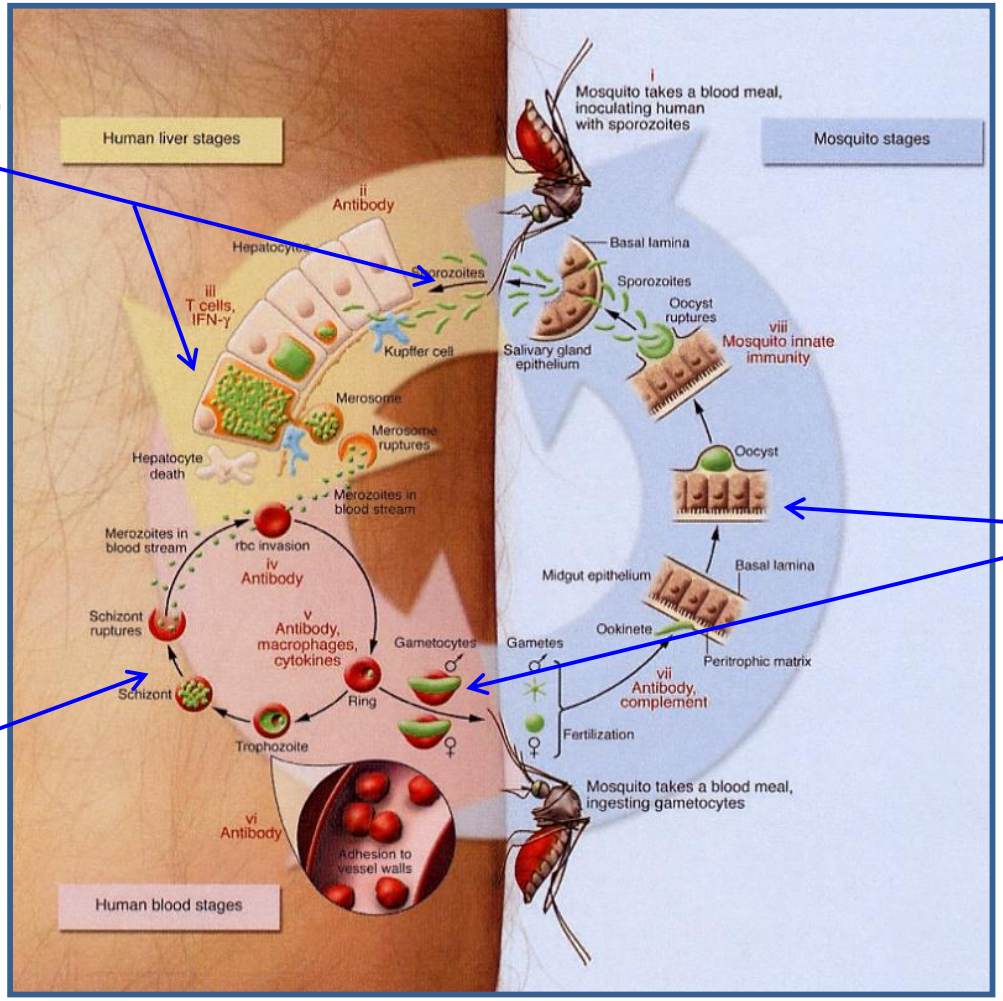
- **Development of malaria vaccines that reduce transmission of the parasite and thereby substantially reduces the incidence of human malaria infection.**



Second edition (2013)

MALARIA VACCINES

Pre-erythrocytic vaccines



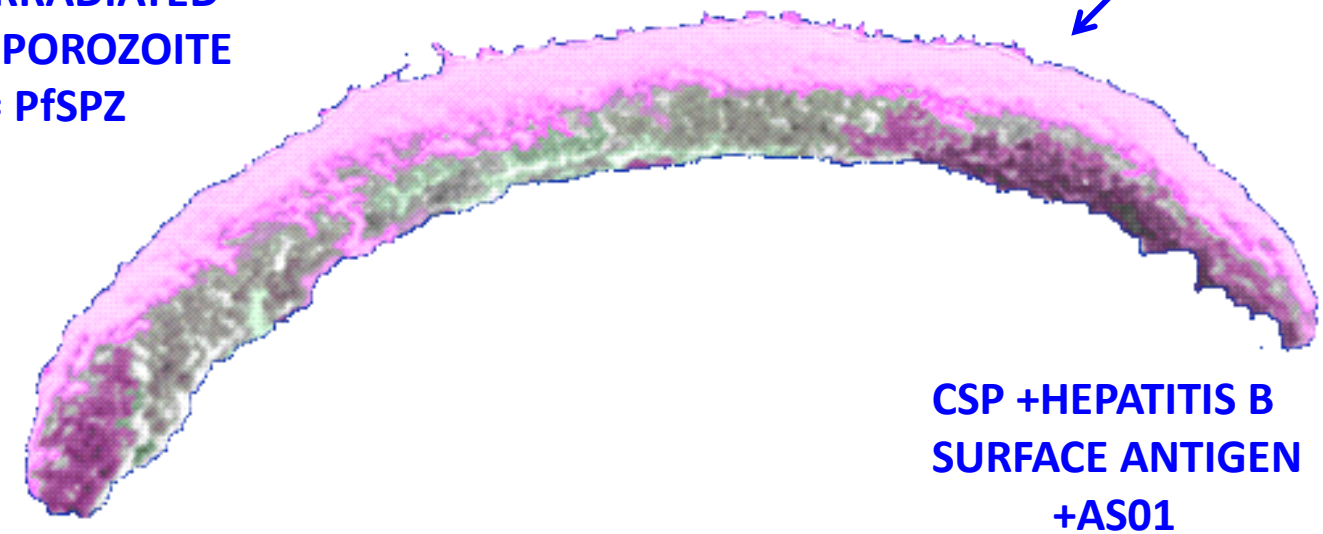
Vaccines that block transmission

Blood-stage vaccines

Plasmodium falciparum - sporozoite

The Circumsporozoite Protein (CSP)

IRRADIATED
SPOROZOITE
= PfSPZ



CSP +HEPATITIS B
SURFACE ANTIGEN
+AS01
= RTSS/AS01

THE CURRENT SITUATION

The two most advanced vaccines

	RTS,S/AS01	PfSPZ
Efficacy		
- Early	> 70%	Up to 100%
- Late	+/-30% at 4 years	??
Strain specificity	Concerns	??
Compatibility with EPI	Partial	?
Route of administration	IM	IV
Safety	Febrile convulsions, ? meningitis ? female mortality	? Break through infections
Cost	?	?

FACTORS TO CONSIDER IN DEPLOYMENT OF AN IMPERFECT MALARIA VACCINE

- **Epidemiological factors**
  - **the burden of infection**
  - **the seasonality of infection.**
- **The risk benefit analysis.**
- **Cost versus other interventions.**
- **The acceptability of vaccination by the target population.**

POTENTIAL USES OF A PARTIALLY EFFECTIVE MALARIA VACCINE

- Vaccination in high burden areas where malaria control has not been achieved.
- Vaccination in areas where malaria transmission is highly seasonal.*
- Elimination campaigns.*
- Halting an epidemic.*

* Efficacy needs to be only be short lasting

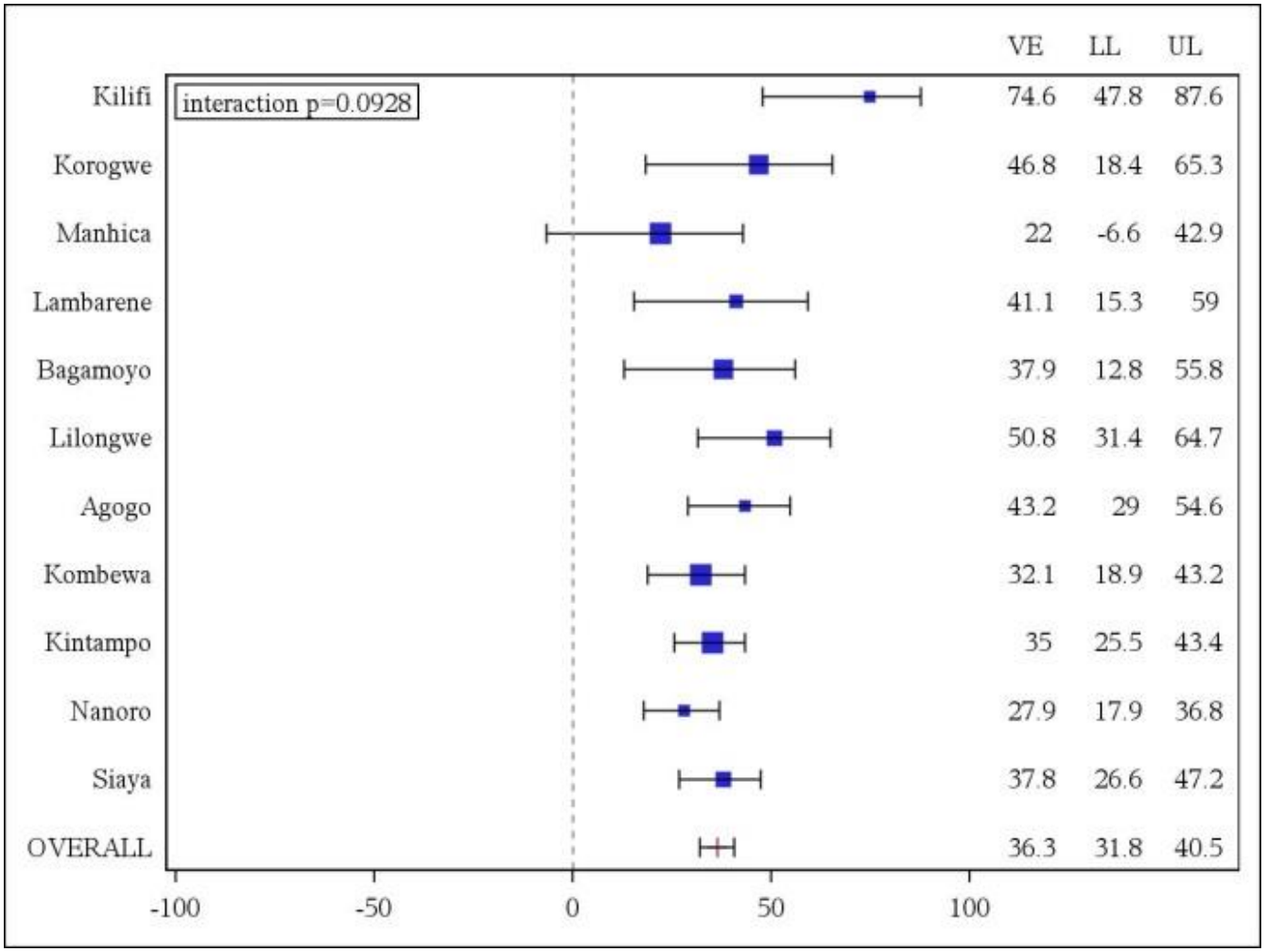
EFFICACY OF RTS,S/AS01 AGAINST CLINICAL MALARIA BY SITE

5-17 month age group

Low

Transmission intensity

High

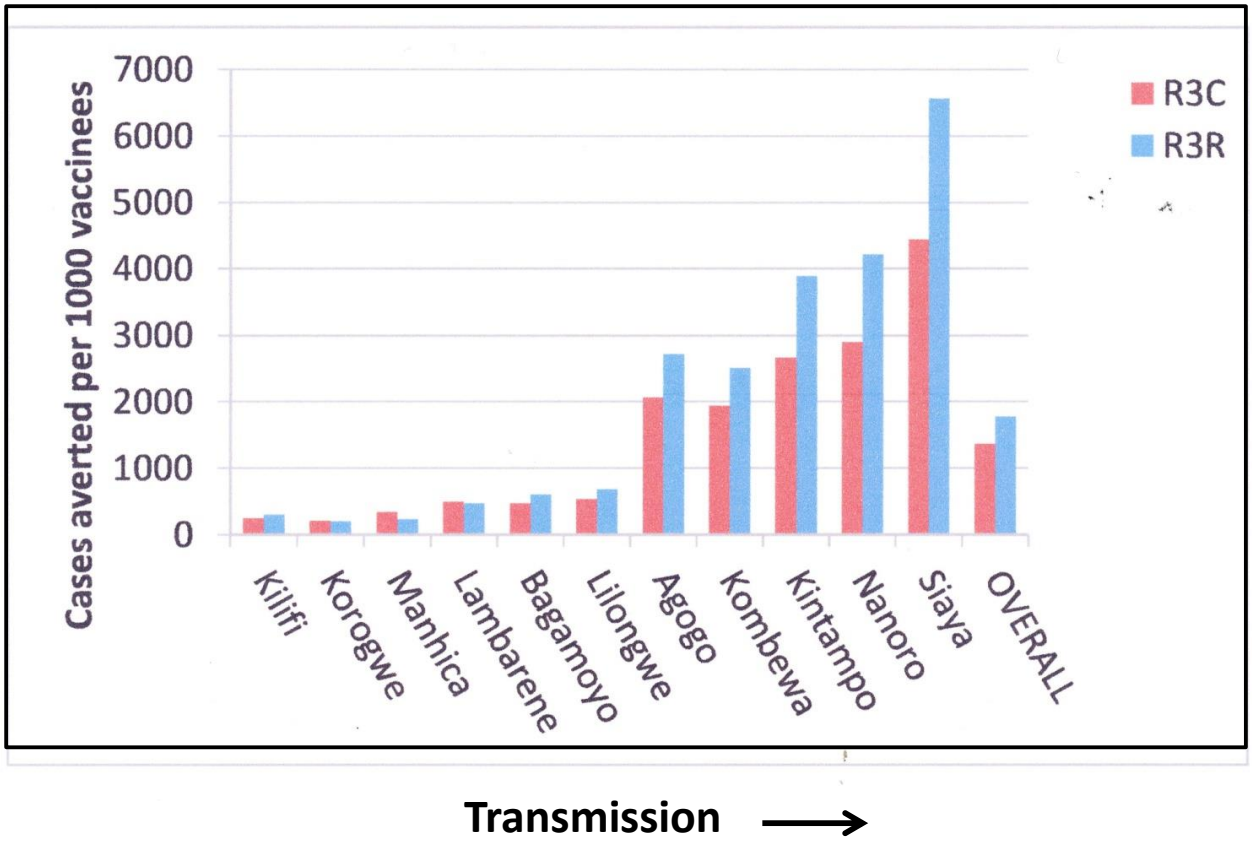


(RTS,S Clinical Trials Partnership. Lancet 2015: 386:31-45)

THE RTS,S PHASE 3 TRIAL

5-17 month age group

Cases prevented per 1,000 vaccinated



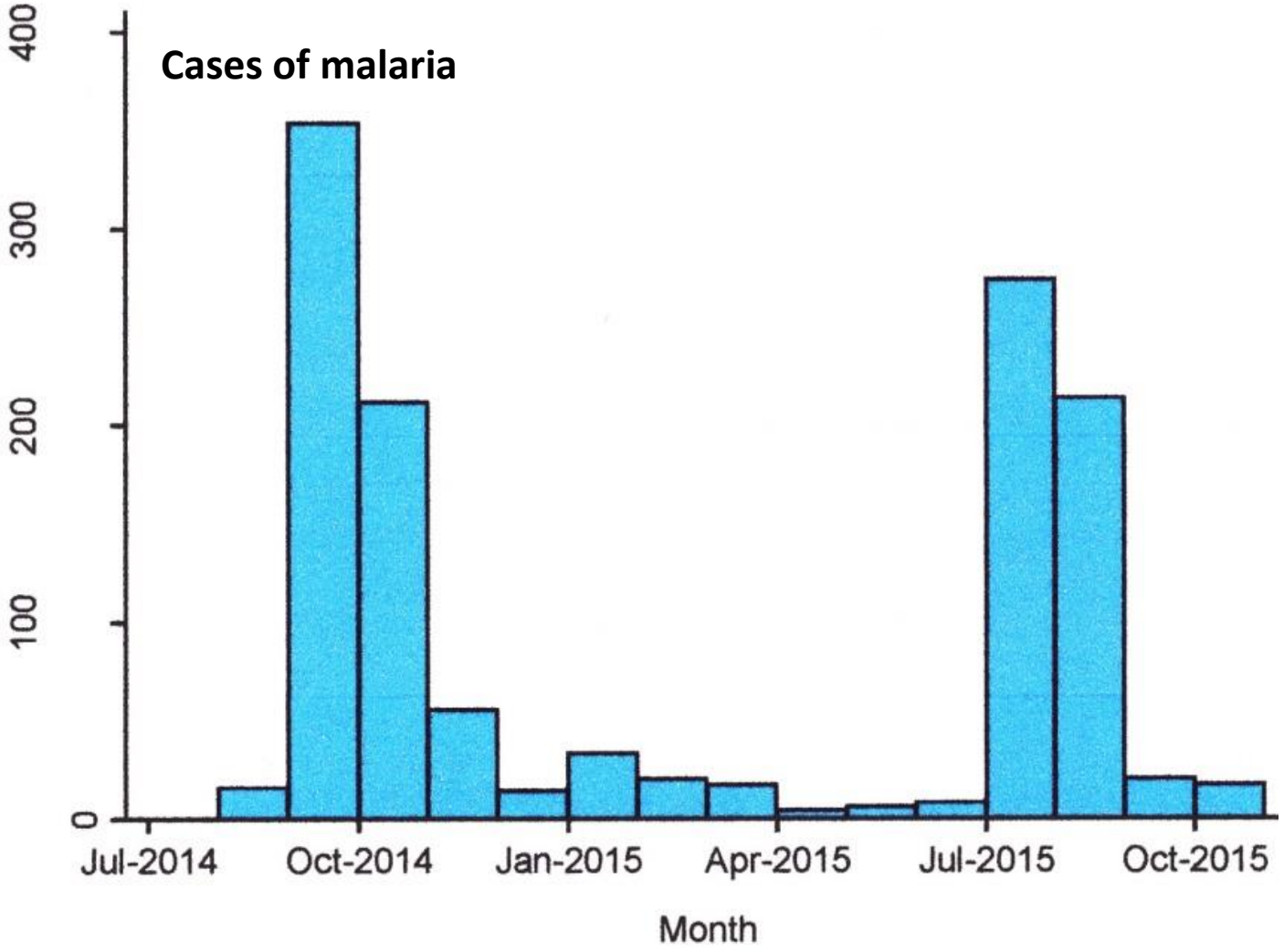
Cases ↑

Transmission →

(RTS,S Clinical Trials Partnership. Lancet 2015: 386:31-45)

VACCINATION IN AREAS OF SEASONAL MALARIA

Hounde, Burkina Faso



(Unpublished data)

SEASONAL MALARIA CHEMOPREVENTION

18 million children likely to receive SMC in 2016

malaria consortium
disease control, better health

UNITAID

(www.access-smc.org)

CHALLENGES TO SEASONAL MALARIA CHEMOPREVENTION

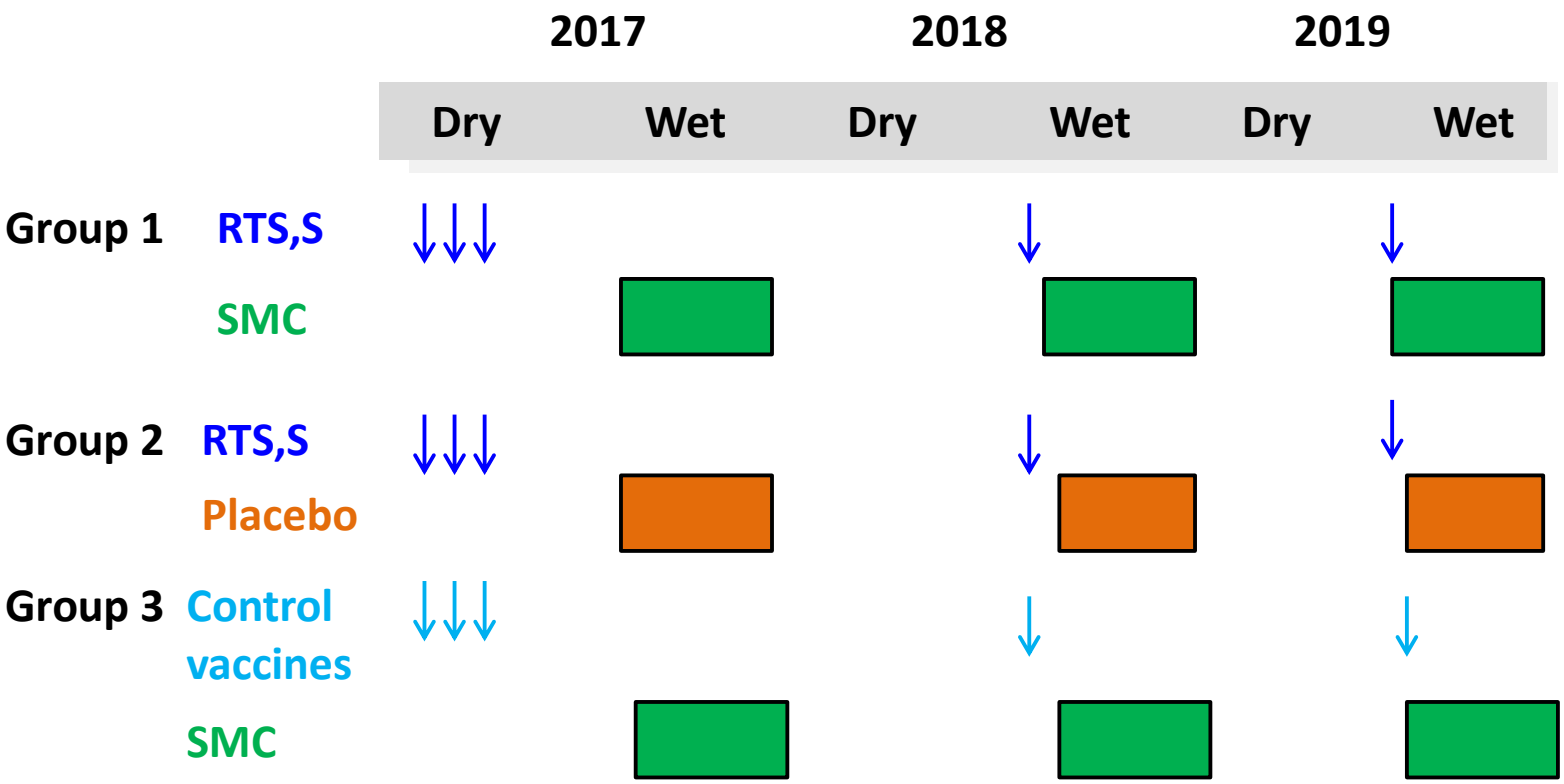
- **Requires many health provider contacts.**
- **Threatened by drug resistance.**
- **No obvious drug replacement.**

COULD SEASONAL VACCINATION

REPLACE SMC?

PROPOSED TRIAL OF SEASONAL VACCINATION WITH RTS,S

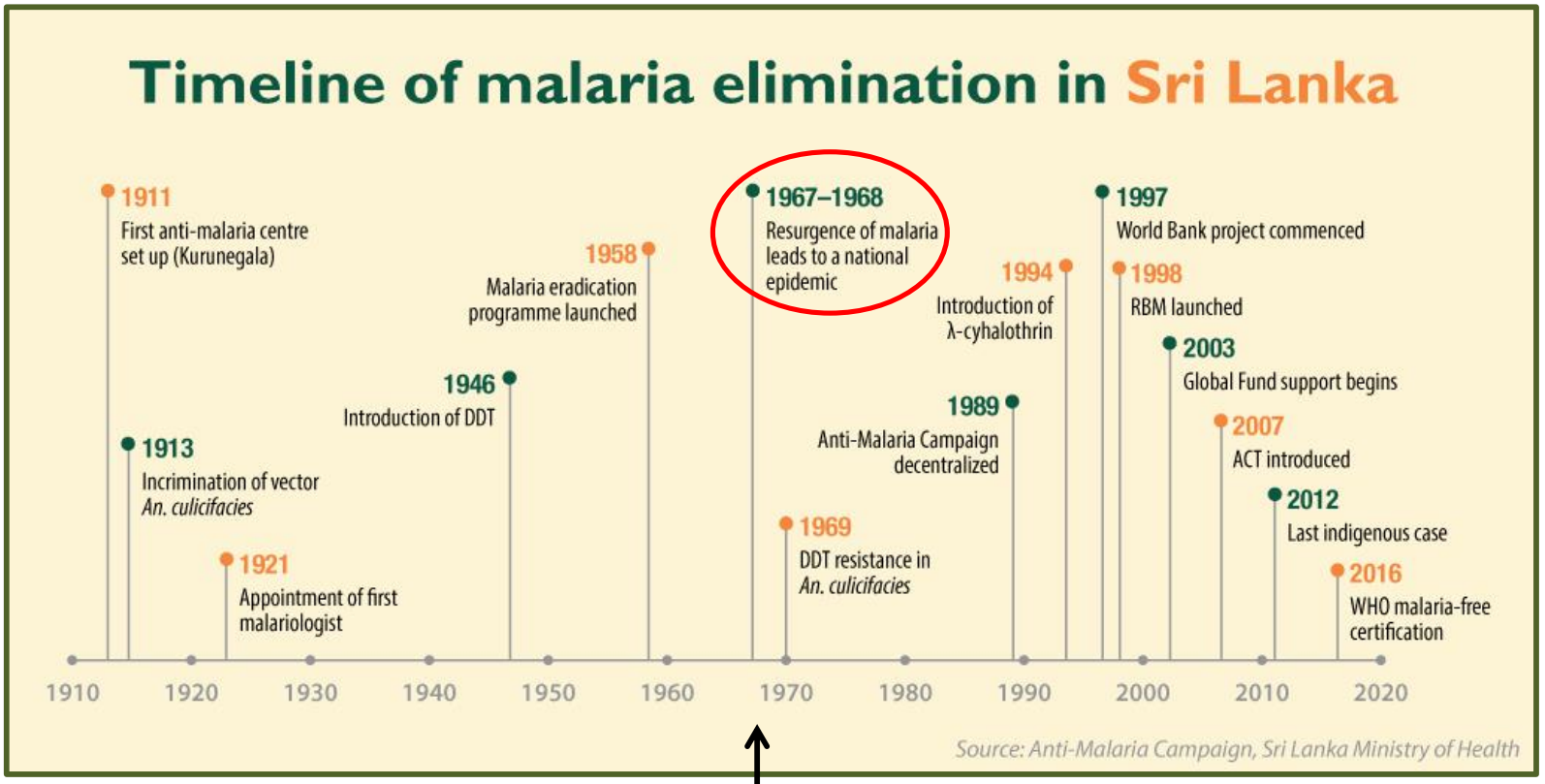
Burkina Faso and Mali



ELIMINATION - BIOKO ISLAND

Planned use of the PfSPZ vaccine for elimination.

HALTING EPIDEMICS



Vaccination

RISK/BENEFIT ANALYSIS

RTS,S/AS01 5- 17 MONTH AGE GROUP

Benefits

36% protection against clinical malaria for 4 years.

Risks

Febrile convulsions.

A possible increase in meningitis.

A possible increase in cerebral malaria.

A possible increase in female deaths.

ACCEPTABILITY AND COST

ACCEPTABILITY

Preference of the community for vaccination compared with other interventions

COST

Cost in reducing disease burden compared with other interventions

CONCLUSION

The first generation of malaria vaccines is likely to have limited efficacy and/or provide only a limited period of protection. Their deployment will need to be targeted at situations matched to their properties so as to ensure their maximum public health benefit.

BACK-UP SLIDES

THE RTS,S PHASE 3 TRIAL

Efficacy against clinical malaria

Time interval of follow-up	Unadjusted Vaccine Efficacy R3C vs C3C (no booster)	R3R vs C3C (booster)*
6-12 week infants		
Month 0 - month 20	27.0% (21.1,32.5)	
Month 21 to study end	7.6% (-0.8,15.3)	23.5% (16.4,30.1)
Month 0 - study end	18.3% (11.7, 24.4)	25.9% (19.9, 31.5)
5-17 month old children		
Month 0 - month 20	45.1% (41.4, 18.7)	
Month 21 to study end	11.4% (4.4,18.0)	25.6 (19.4, 31.3)
Month 0 - study end	28.3% (23.3,32.9)	36.3% (31.8,40.5)

* Booster at 20 months

(RTS,S Clinical Trials Partnership. Lancet 2015: 386:31-45)

THE RTS,S PHASE 3 TRIAL

Risks

Specific to RTS,AS01

- Febrile convulsions.
- Increased mortality in female children.
- Increased risk of meningitis (5-17 month group).

A risk for any variant vaccine

- Vaccine escape.

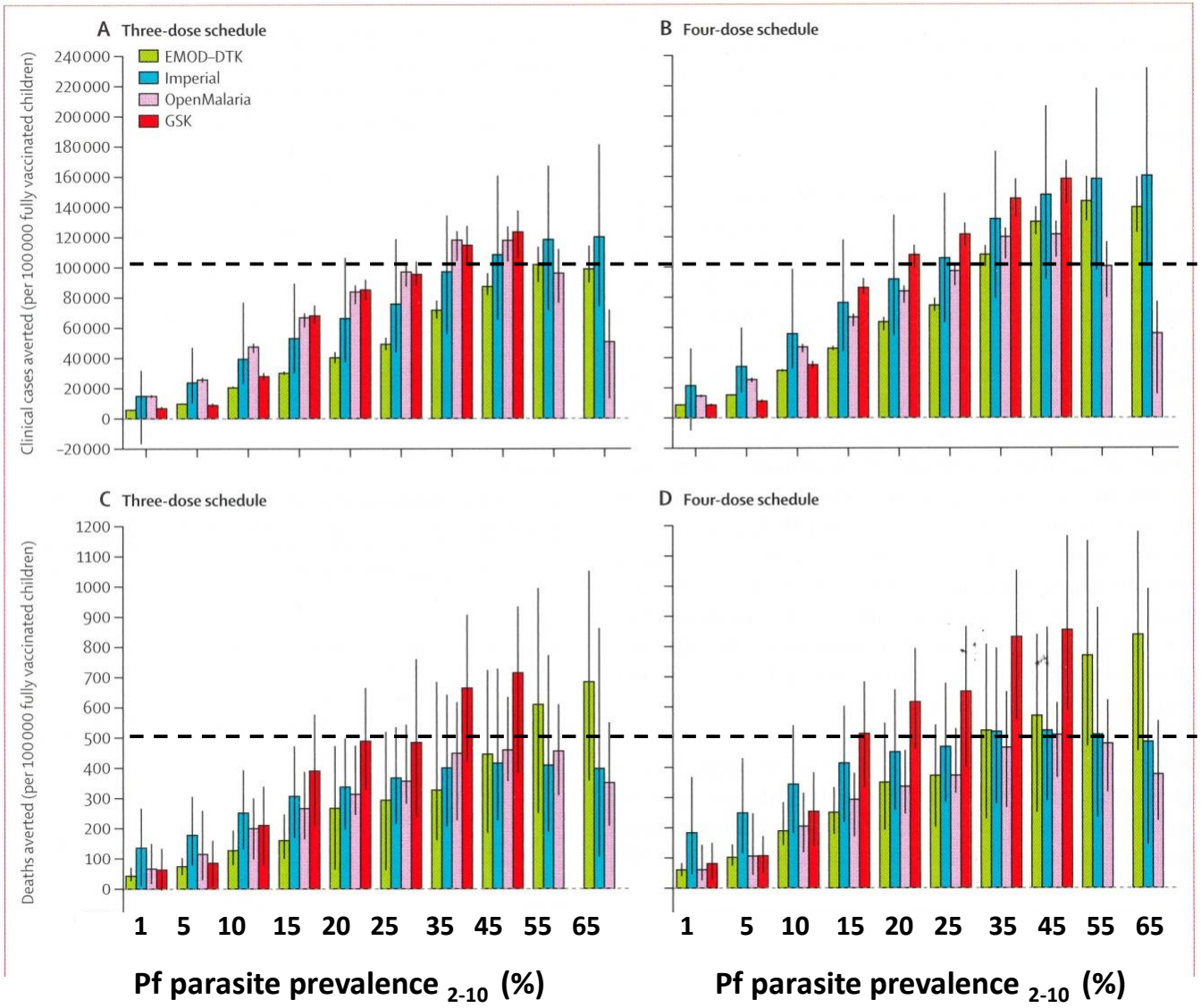
A risk for any successful malaria control measure

- ‘Rebound’ in malaria.
- Increased risk of cerebral malaria (5-17 month group).

MODELED IMPACT OF RTS,S/AS01

Cases prevented per 100,000 vaccinated

Deaths prevented per 100,000 vaccinated

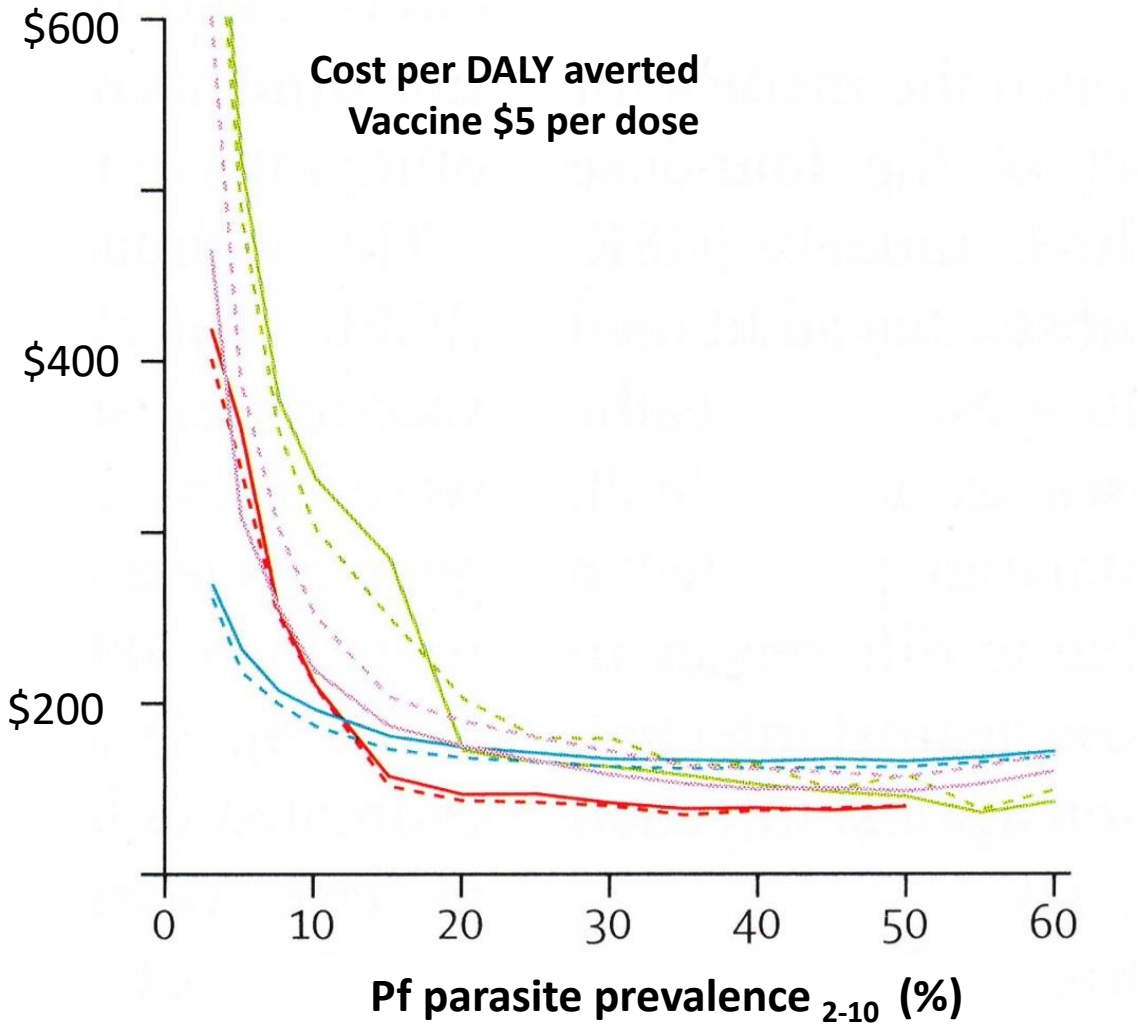


100,000

500

(Penny et al. Lancet 2016;387:367-75)

COST EFFECTIVENESS OF RTS,S/AS01



(Penny et al. Lancet 2016;387:367-75)

INDIRECT IMPACT OF MALARIA CONTROL

- **Reduction in invasive bacterial infections, especially non-typhoidal salmonella infection.**
- **Improvement in nutrition.**
- **Improvement in school attendance and performance.**
- **Improvement in productivity.**