

# The role of clinical trials in strengthening research centers in Africa

Pedro L. Alonso

Hospital Clinic / Universidad de Barcelona

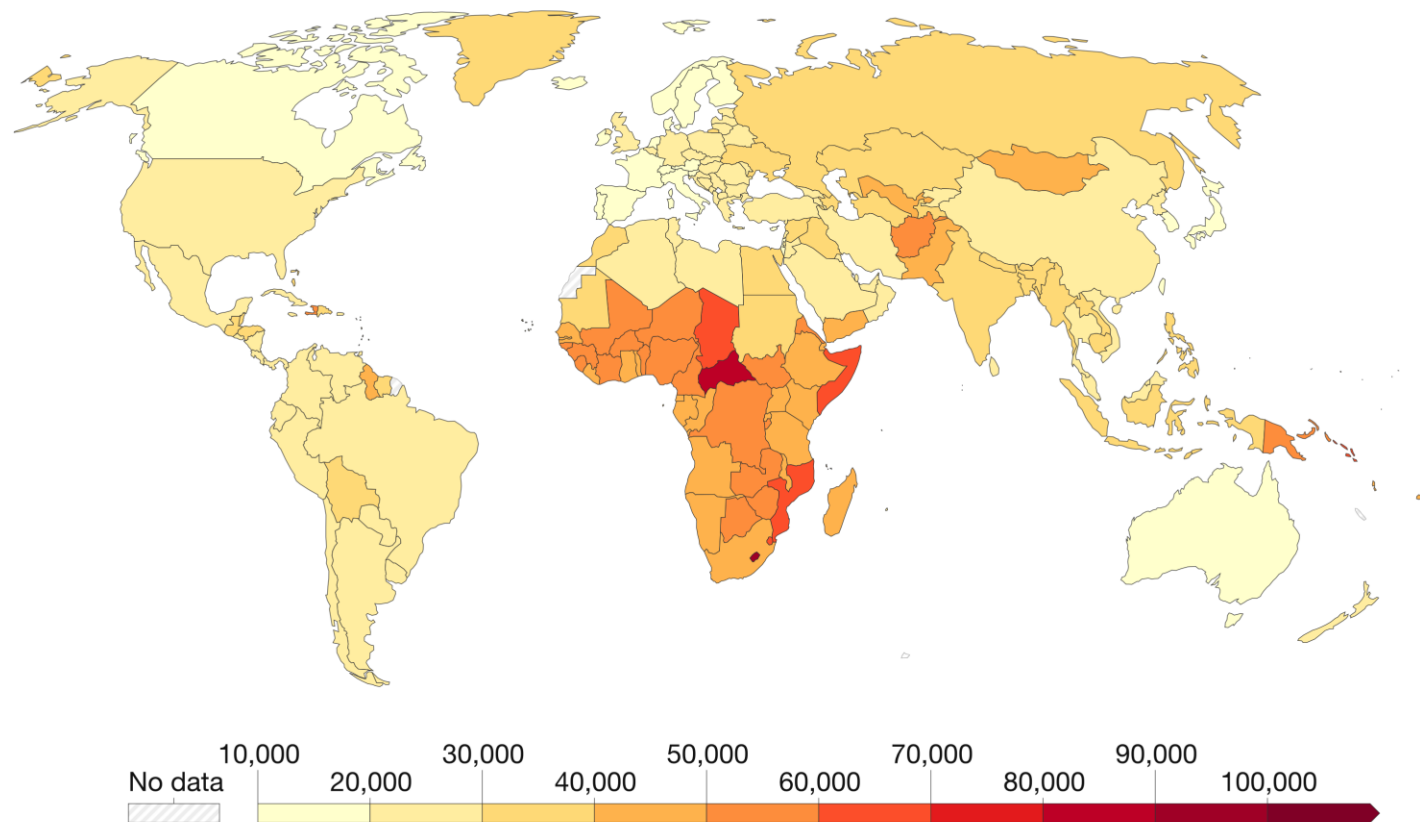
&

Manhiça Health Research Center

# Burden of disease, 2019

Our World  
in Data


Disability-Adjusted Life Years (DALYs) per 100,000 individuals from all causes. DALYs measure the total burden of disease – both from years of life lost due to premature death and years lived with a disability. One DALY equals one lost year of healthy life.



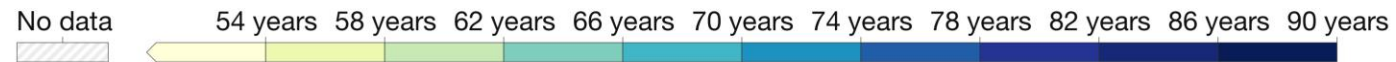
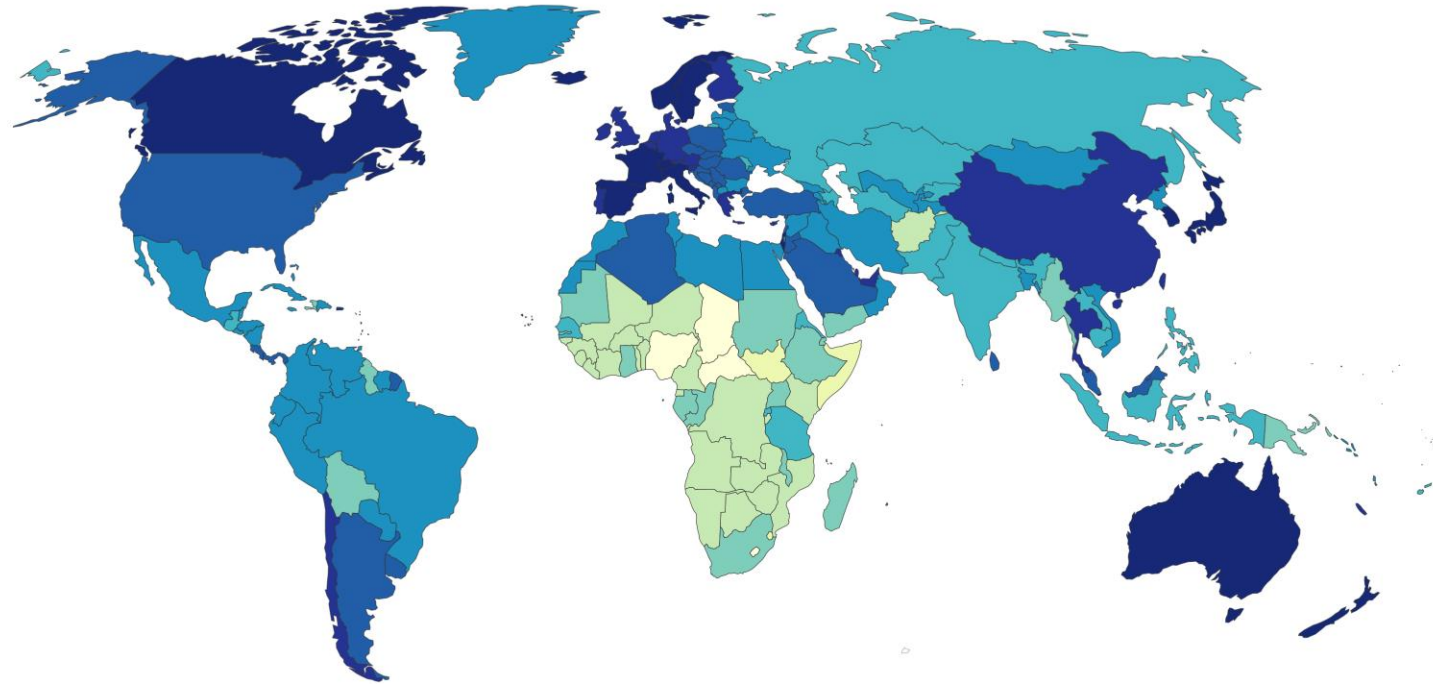
Source: IHME, Global Burden of Disease (2019)

[OurWorldInData.org/burden-of-disease](https://OurWorldInData.org/burden-of-disease) • CC BY

Note: To allow comparisons between countries and over time this metric is age-standardized<sup>1</sup>.

**1. Age standardization:** Age standardization is an adjustment that makes it possible to compare populations with different age structures, by standardizing them to a common reference population.  Read more: [How does age standardization make health metrics comparable?](#)

## Life expectancy, 2021



Source: UN WPP (2022); Zijdeman et al. (2015); Riley (2005)

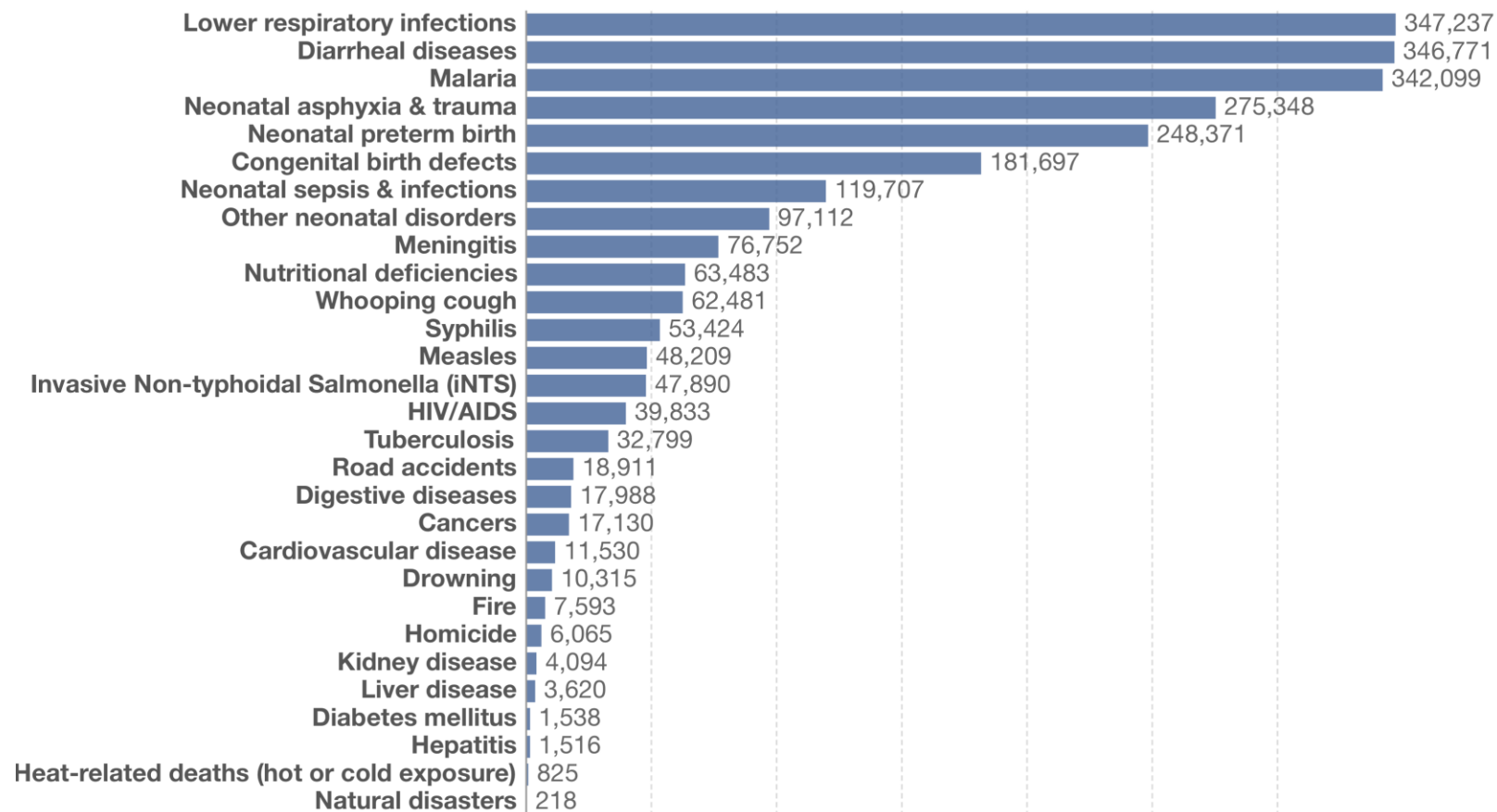
OurWorldInData.org/life-expectancy • CC BY

Note: Shown is the 'period life expectancy'. This is the average number of years a newborn would live if age-specific mortality rates in the current year were to stay the same throughout its life.

## Causes of death in children under five, African Region (WHO), 2019



Shown are estimates of the annual number of deaths from each cause, published by the IHME. Estimates come with wide uncertainties especially for countries with poor vital registration.



Source: IHME, Global Burden of Disease (2019)

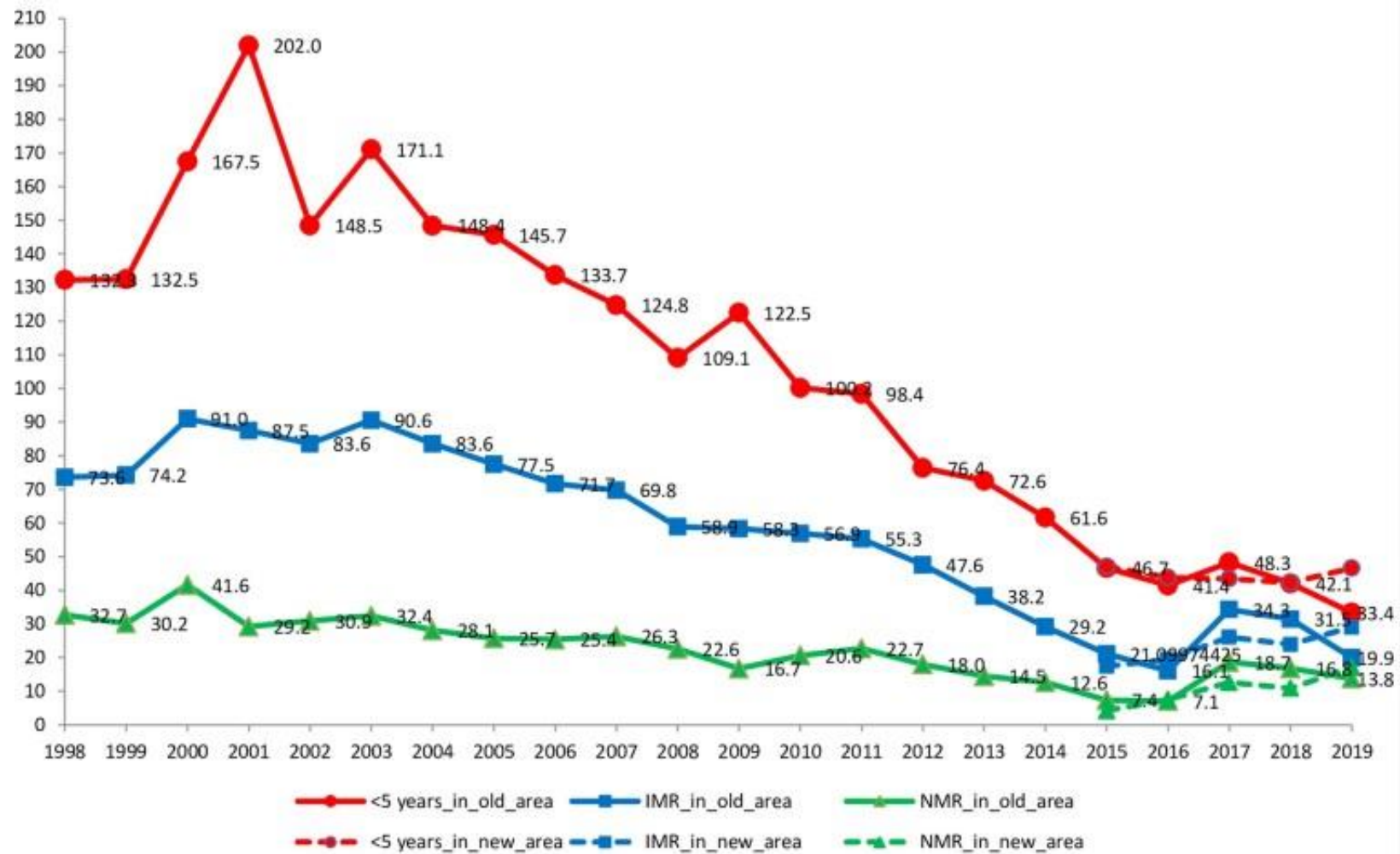
OurWorldInData.org/causes-of-death • CC BY

# The need for medical research in Africa

- The unfinished agenda of Global Health
- The 10/90 gap
  - Funding of health priorities
  - The 10/90 gap also reflects disparities in research infrastructure, capacity, and expertise between high-income countries and low- and middle-income countries. Limited access to resources, including laboratories, trained researchers, and clinical trial facilities, hampers the ability of developing countries to conduct their research and address their specific health challenges.

# The medical research ecosystem

- Universities and research centers
- Research funding
- Collaborative networks and partnerships
- Health data and information systems
- Capacity building and training
- Research ethics and regulations
- Infrastructure and technology
- Translational research and implementation science
- Regulatory environment



**Malaria**

HIV/AIDS

**TB**

Pneumonias  
and  
other IBDs

**Diarrheal  
diseases**

Other areas

Maternal and Reproductive Health

**Clinical and molecular Epidemiology**

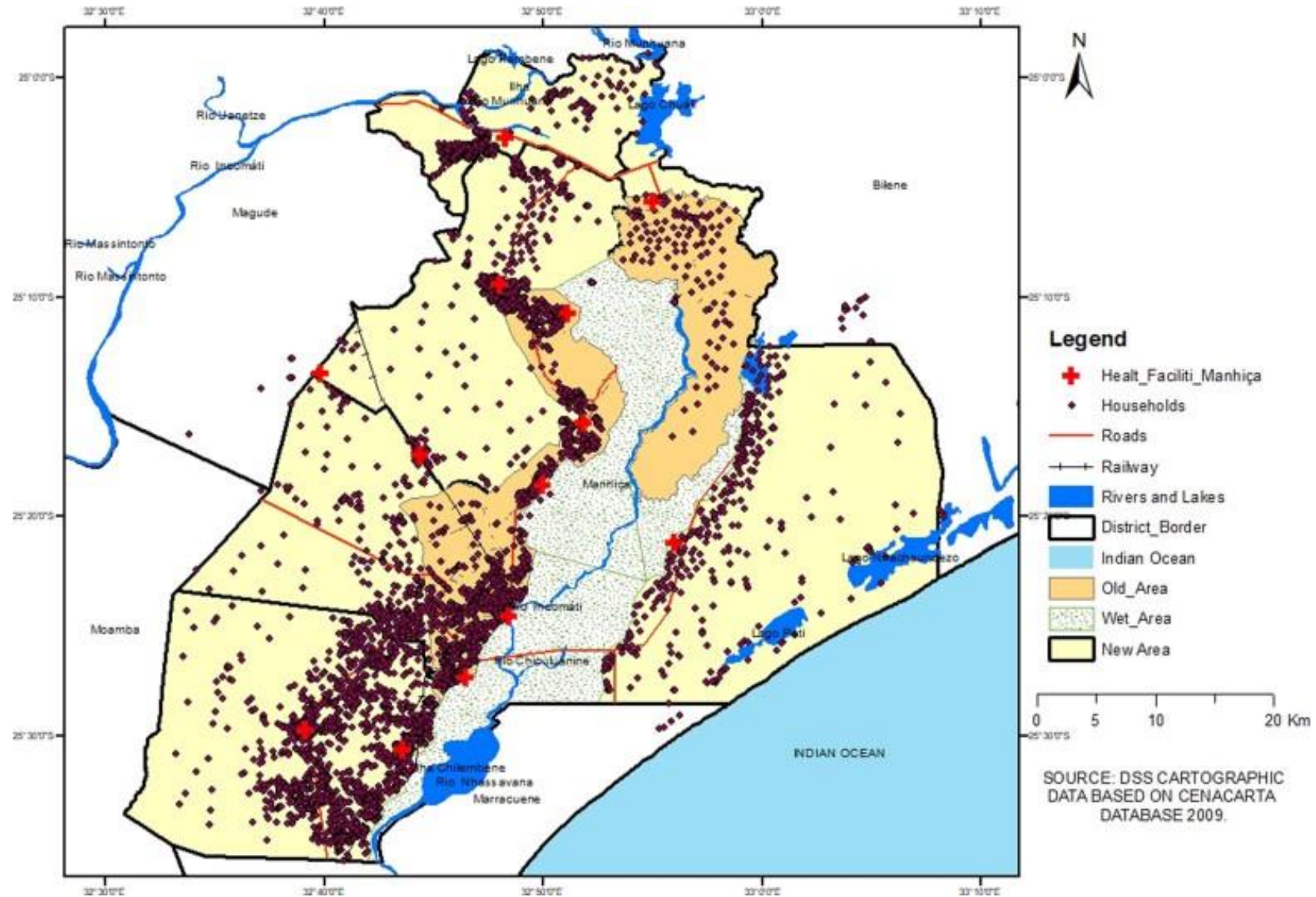
Immunology and Pathophysiology

**Evaluation of Drugs and Vaccines**

Monitoring and Evaluation

**Social Sciences**





Insecticide-treated bed nets ("mosquito nets") may be a relatively cheap and acceptable method of reducing man-vector contact.<sup>2,3</sup> However, the efficacy of insecticide-

weekly either chemoprophylaxis with maloprim or a placebo throughout the malaria transmission season. We measured mortality in children in PHC villages before and after the interventions described, and compared this with mortality in villages where no interventions occurred (non-PHC villages).

About 92% of children in PHC villages slept under insecticide-treated bed nets. In the year before intervention, mortality in children aged 1-4 years was

Research on Cancer, Lyon, France (A. J. Hall, MRCP). Correspondence to: Dr P. L. Alonso, Institute de Parasitologia "Lopez Neyra", Ventanilla, 11. 18001 Granada, Spain.

nets on mortality.

Studies in the Farafenni area of The Gambia showed that morbidity from malaria was reduced by targeted chemoprophylaxis with maloprim (pyrimethamine and dapsone) and the use of permethrin-impregnated bed nets, and that each of these malaria-control strategies can be used in a village-based primary health-care (PHC) scheme.<sup>5,6</sup> Therefore, we have done a field study to determine whether insecticide treatment of bed nets could be implemented on a

TABLE I—MORTALITY RATES FOR INFANTS (DEATHS/1000 LIVE BIRTHS) AND CHILDREN AGED 1-4 (DEATHS/1000 PER YEAR) FOR 1 YEAR BEFORE AND AFTER INTERVENTION

Age (yr)	PHC villages	Non-PHC villages	Rate ratio PHC/non-PHC (95% CI)	p*
<i>Pre-intervention</i>				
<1	115.5 (65/563)†	127.1 (46/362)†	0.91 (0.64-1.29)	NS
1-4	47.6 (81/1700)‡	31.5 (37/1176)‡	1.51 (1.03-2.22)	0.03
5q0§	267.5	224.6	..	..
<i>Post-intervention</i>				
<1	73.5 (41/558)†	105.1 (37/352)†	0.7 (0.46-1.07)	NS
1-4	9.0 (16/1787)‡	24.2 (30/1240)‡	0.37 (0.2-0.68)	0.001
5q0§	104.4	186.7	..	..

\* $\chi^2$  test, NS = not significant. †Deaths/live births; ‡deaths/approximate mid-year population. §Of 1000 live births, this is an estimate of the number that do not live until 5 years old.

residents, it was important to determine whether mortality rates differed between them before intervention started. Past levels of mortality in children under 5 years old in the two sets of villages are shown in fig 1. Mortality rates over the past 15 years have followed a convergent and then a

# Intermittent preventive antimalarial treatment for Tanzanian infants: follow-up to age 2 years of a randomised, placebo-controlled trial

David Schellenberg, Clara Menendez, John Japonte, Elizaus Kahigwa, Marcel Tanner, Hassan Mshinda, Pedro Alonso



Lancet 2005; 365: 1481–83  
See [Comment](#) page 1443

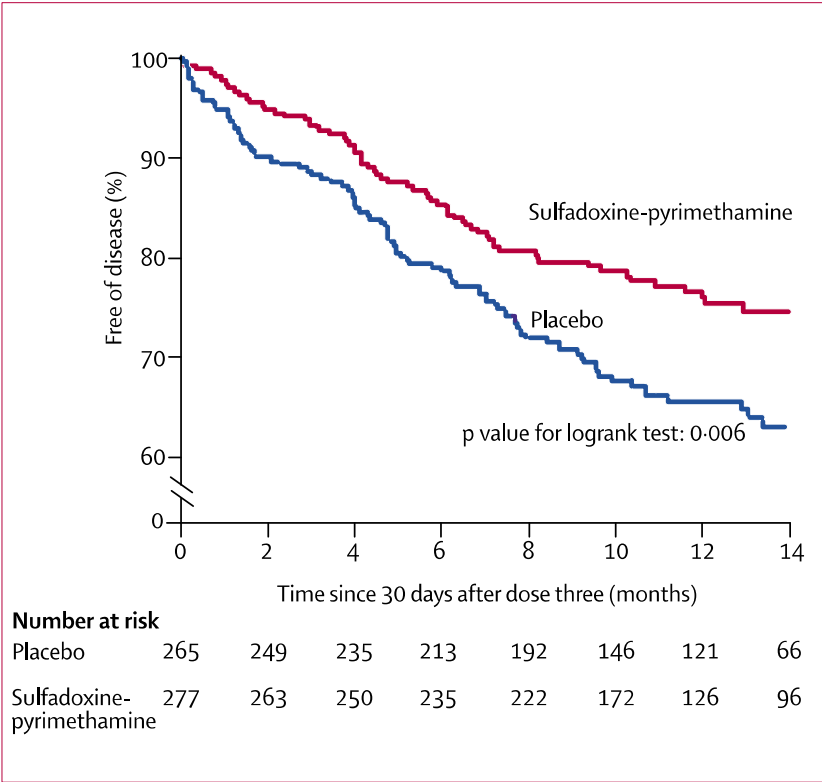
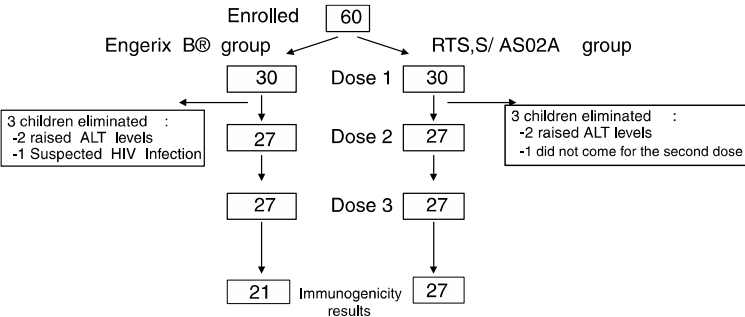


Figure: Kaplan-Meier survival curve

# Safety and immunogenicity of the RTS,S/AS02A candidate malaria vaccine in children aged 1–4 in Mozambique

E. Macete<sup>1,2,3</sup>, J. J. Aponte<sup>1,2</sup>, C. Guinovart<sup>1,2</sup>, J. Sacarlal<sup>1,2,4</sup>, O. Ofori-Anyinam<sup>5</sup>, I. Mandomando<sup>1,2,6</sup>, M. Espasa<sup>1,2,6</sup>, C. Bevilacqua<sup>5</sup>, A. Leach<sup>5</sup>, M. C. Dubois<sup>5</sup>, D. G. Heppner<sup>7</sup>, L. Tello<sup>1,2</sup>, J. Milman<sup>8</sup>, J. Cohen<sup>5</sup>, F. Dubovsky<sup>8</sup>, N. Tornieporth<sup>5</sup>, R. Thompson<sup>1,4,6</sup> and P. L. Alonso<sup>1,2,6</sup>



**Table 3** Incidence of solicited general symptoms (no unsolicited symptoms are listed in this table) within the 4-day follow-up

	Dose 1		Dose 2		Dose 3		Dose 3		Dose 3		Dose 3	
	Engerix-B (N = 30)	RTS,S/ AS02A (N = 30)	Engerix-B (N = 27)	RTS,S/ AS02A (N = 27)	Engerix-B (N = 26)	RTS,S/ AS02A (n = 27)	Engerix-B (N = 26)	RTS,S/ AS02A (n = 27)	Engerix-B (N = 26)	RTS,S/ AS02A (n = 27)	Engerix-B (N = 26)	RTS,S/ AS02A (n = 27)
	n	%	n	%	n	%	n	%	n	%	n	%
General symptoms												
Drowsiness												
Any	0	0.0	1	3.3	0	0.0	1	3.7	1	3.8	2	7.4
Related	0	0.0	1	3.3	0	0.0	0	0.0	0	0.0	1	3.7
Grade 3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Grade 3 related	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Fever												
Any	2	6.7	4	13.3	0	0.0	4	14.8	1	3.8	4	14.8
Related	1	3.3	2	6.7	0	0.0	3	11.1	0	0.0	3	11.1
Grade 3	0	0.0	1	3.3	0	0.0	0	0.0	0	0.0	0	0.0
Grade 3 related	0	0.0	1	3.3	0	0.0	0	0.0	0	0.0	0	0.0
Irritability												
Any	0	0.0	2	6.7	1	3.7	2	7.4	1	3.8	2	7.4
Related	0	0.0	1	3.3	0	0.0	2	7.4	0	0.0	1	3.7
Grade 3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Grade 3 related	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Loss of appetite												
Any	0	0.0	1	3.3	0	0.0	2	7.4	1	3.8	7	25.9
Related	0	0.0	1	3.3	0	0.0	2	7.4	0	0.0	3	11.1
Grade 3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Grade 3 related	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Local symptoms												
Pain												
Any	2	6.7	2	6.7	0	0.0	4	14.8	1	3.8	19	70.4
Grade 3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.7
Swelling												
Any	16	53.3	23	76.7	14	51.9	16	59.3	7	26.9	24	88.9
Grade 3	0	0.0	4	13.3	0	0.0	1	3.7	0	0.0	14	51.9

N<sub>i</sub>, number of subjects with at least one symptom sheet completed; n, number of subjects reporting a specified symptom; %, percentage of subjects reporting a specified symptom.

Research

Open Access

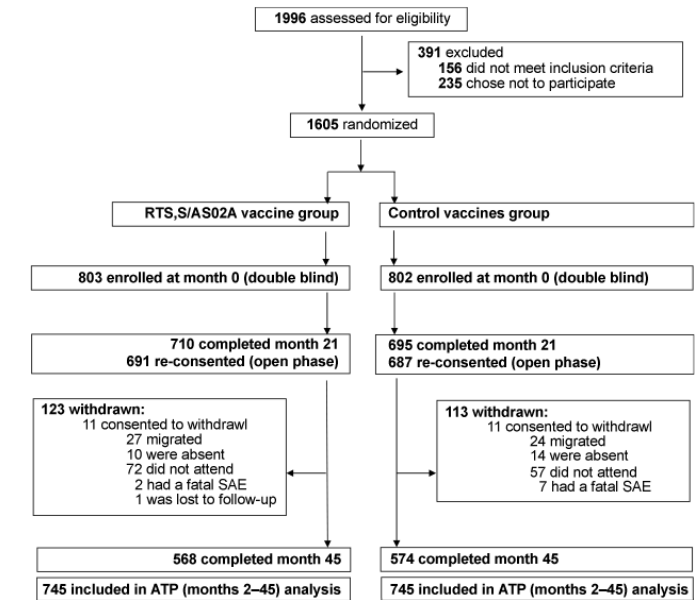
## Evaluation of two formulations of adjuvanted RTS, S malaria vaccine in children aged 3 to 5 years living in a malaria-endemic region of Mozambique: a Phase I/IIb randomized double-blind bridging trial

Eusebio V Macete<sup>\*1,2,3</sup>, Jahit Sacarlal<sup>1,4</sup>, John J Aponte<sup>1,2</sup>, Amanda Leach<sup>6</sup>, Margarita M Navia<sup>1,2</sup>, Jessica Milman<sup>7</sup>, Caterina Guinovart<sup>1,2</sup>, Inacio Mandomando<sup>1,5</sup>, Yolanda López-Púa<sup>2</sup>, Marc Lievens<sup>6</sup>, Alex Owusu-Ofori<sup>6</sup>, Marie-Claude Dubois<sup>6</sup>, Conor P Cahill<sup>6</sup>, Marguerite Koutsoukos<sup>6</sup>, Marla Sillman<sup>7</sup>, Ricardo Thompson<sup>1,4,5</sup>, Filip Dubovsky<sup>7</sup>, W Ripley Ballou<sup>6</sup>, Joe Cohen<sup>6</sup> and Pedro L Alonso<sup>1,2</sup>

# Long-Term Safety and Efficacy of the RTS,S/AS02A Malaria Vaccine in Mozambican Children

Jahit Sacarlal,<sup>1,2,5</sup> Pedro Aide,<sup>1,3</sup> John J. Aponte,<sup>1,5</sup> Montse Renom,<sup>1,5</sup> Amanda Leach,<sup>6</sup> Inácio Mandomando,<sup>1,3</sup> Marc Lievens,<sup>6</sup> Quique Bassat,<sup>1,5</sup> Sarah Lafuente,<sup>1,5</sup> Eusébio Macete,<sup>1,4</sup> Johan Vekemans,<sup>6</sup> Caterina Guinovart,<sup>1,5</sup> Betuel Sigauque,<sup>1,3</sup> Marla Sillman,<sup>7</sup> Jessica Milman,<sup>7</sup> Marie-Claude Dubois,<sup>6</sup> Marie-Ange Demoitié,<sup>6</sup> Joelle Thonnard,<sup>6</sup> Clara Menéndez,<sup>1,5</sup> W. Ripley Ballou,<sup>6,a</sup> Joe Cohen,<sup>6</sup> and Pedro L. Alonso<sup>1,5</sup>

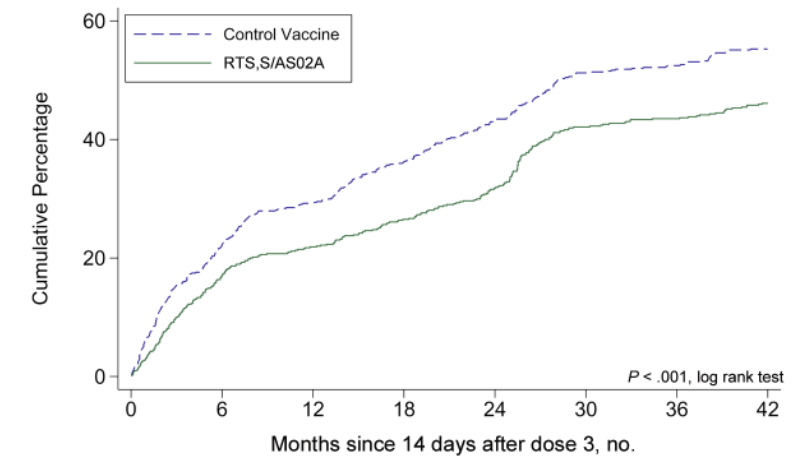
<sup>1</sup>Centro de Investigação em Saúde de Manhiça (CISM) Manhiça, <sup>2</sup>Faculdade de Medicina, Universidade Eduardo Mondlane, <sup>3</sup>Instituto Nacional de Saúde and <sup>4</sup>Direcção Nacional de Saúde, Ministério de Saúde, Maputo, Mozambique; <sup>5</sup>Barcelona Center for International Health Research, Hospital Clínic/Institut d'Investigacions Biomèdiques August Pi i Sunyer, Universitat de Barcelona, Barcelona, Spain; <sup>6</sup>GlaxoSmithKline Biologicals, Rixensart, Belgium; <sup>7</sup>Program for Appropriate Technology in Health, Malaria Vaccine Initiative, Bethesda, Maryland



**Figure 2.** Trial profile for cohort 1. ATP, according-to-protocol analysis; SAE, serious adverse event.

Manhiça Cohort 1 N = 1605	Vaccination	XXX										PCD				
	Blood Sampling	XX	X					X		X	X	X				
Study Month		0	1	2	2½			8	½	21	33	45				
Ilha Josina Cohort 2 N = 417	Blood Sampling	XX	XX	XXXXXX	XXXXXX			XX		X	X					X
	Parasite clearance				d45											
	Vaccination	XX	XX													
Double-blind phase										Single-blind phase			Open phase			

**Figure 1.** Study design. ADI, active detection of information; d45, day 45; double-blind phase, study months 2.5–8; open phase, study months 21–45; PCD, passive case detection; single-blind phase, study months 8–21.



No. at risk								
Control	745	570	512	428	377	324	312	272
RTS,S	745	599	564	496	449	382	373	324

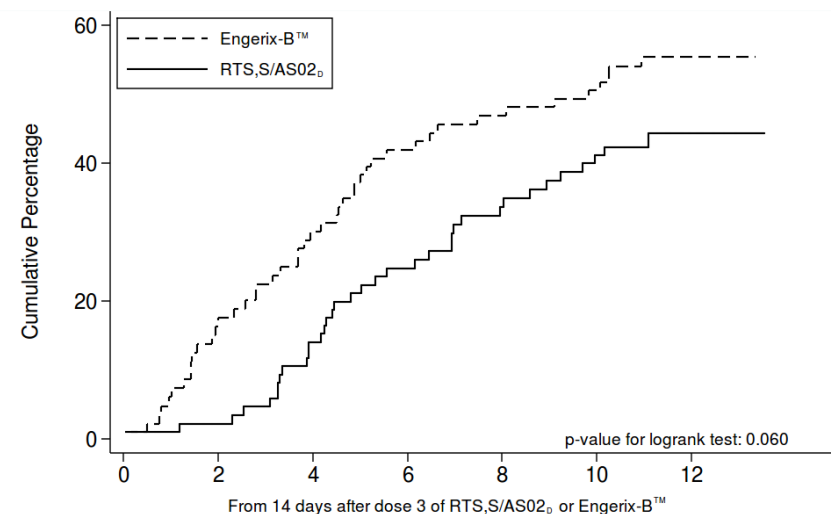
# Safety, Immunogenicity and Duration of Protection of the RTS,S/AS02<sub>D</sub> Malaria Vaccine: One Year Follow-Up of a Randomized Controlled Phase I/IIb Trial

Pedro Aide<sup>1,3\*</sup>, John J. Aponte<sup>1,2</sup>, Montse Renom<sup>1,2</sup>, Tacilta Nhampossa<sup>1,3</sup>, Jahit Sacarlal<sup>1,4</sup>, Inacio Mandomando<sup>1,3</sup>, Quique Bassat<sup>1,2</sup>, Maria Nélia Manaca<sup>1</sup>, Amanda Leach<sup>5</sup>, Marc Lievens<sup>5</sup>, Johan Vekemans<sup>5</sup>, Marie-Claude Dubois<sup>5</sup>, Christian Loucq<sup>6</sup>, W. Ripley Ballou<sup>5</sup>, Joe Cohen<sup>5</sup>, Pedro L. Alonso<sup>1,2</sup>

<sup>1</sup> Centro de Investigação em Saúde da Manhica (CISM), Maputo, Mozambique, <sup>2</sup> Barcelona Centre for International Health Research, Hospital Clinic, University of Barcelona, Barcelona, Spain, <sup>3</sup> Instituto Nacional de Saúde, Ministério de Saúde, Maputo, Mozambique, <sup>4</sup> Faculdade de Medicina, Universidade Eduardo Mondlane, Maputo, Mozambique, <sup>5</sup> Glaxo-SmithKline Biologicals, Rixensart, Belgium, <sup>6</sup> PATH Malaria Vaccine Initiative, Bethesda, Maryland, United States of America

Table 4. Vaccine efficacy evaluated for different follow-up periods.

	Engerix B (n = 92)				RTS,S/AS02 <sub>D</sub> (n = 93)		Vaccine Efficacy		
	Events	PYAR	Rate	Events	PYAR	Rate	95% CI		p
ATP <sub>(3-9)</sub>									
First or only (FO) episode of fever and parasitemia . 500/ml	34	31.5	1.08	21	38.2	0.55	48.8%	11.3–70.4	0.017
FO episode of fever or history of fever* and parasitemia . 0/ml	48	27.7	1.74	29	36.4	0.80	54.5%	27.3–71.5	0.001
Multiple episodes of fever and parasitemia. 500/ml	45	36.2	1.24	23	40.2	0.57	53.7%	21.4–72.7	0.004
Multiple episodes of fever or history of fever* and parasitemia . 0/ml	72	36.0	2.00	34	40.0	0.85	58.9%	35.8–73.6	, 0.001



# Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial



Pedro L Alonso, Jihit Sacarlal, John J Aporo, Amanda Leach, Eusebio Macete, Jessica Milman, Inacio Mandomando, Bart Spiessens, Caterina Guinovart, Mateu Espasa, Quique Bassat, Pedro Aide, Otokua Ofori-Aryinam, Margarita M Navia, Sabine Corachan, Marc Cauppens, Marie-Gaude Dubois, Marie-Ange Demoté, Filip Dubovsky, Clara Menéndez, Nadia Tomieporoth, W Riple Ballou, Ricardo Thompson, Joe Cohen

Lancet 2004; 364: 1411–20

See Comment page 1380

Centre de Salut Internacional,

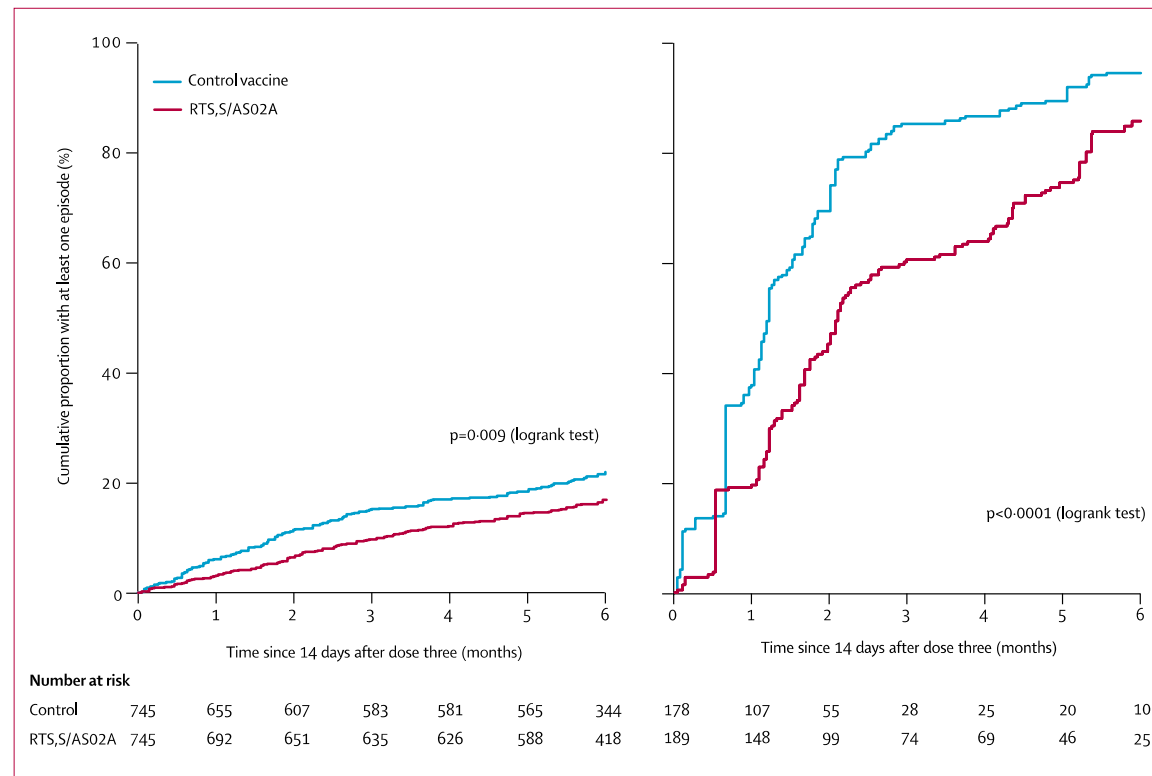
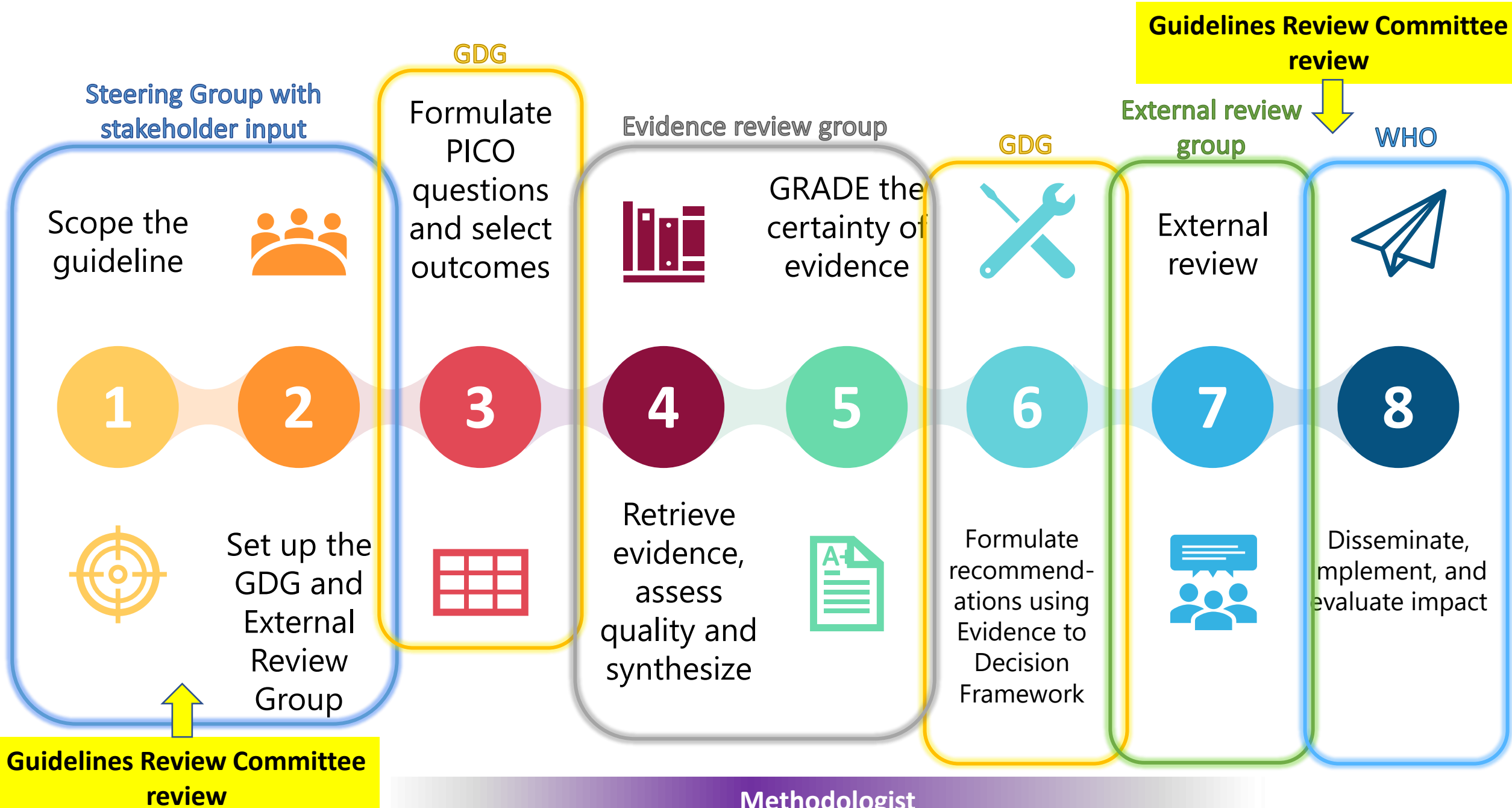


Figure 4: Kaplan-Meier curves for cumulative proportion with at least one episode of clinical malaria (left) or malaria infection (right)





# WHO malaria vaccine position paper

March 2022

<https://www.who.int/publications/i/item/WHO-2022-97-61-60>

2022, 97, 61-60



World Health Organization

Organisation mondiale de la Santé

No 9

Weekly epidemiological record

Relevé épidémiologique hebdomadaire

4 MARCH 2022, 97th YEAR / 4 MARS 2022, 97<sup>e</sup> ANNÉE

No 9, 2022, 97, 61-60

<http://www.who.int/wer>

Contents

61 Malaria vaccine: WHO position paper – March 2022

76 Monthly report on dengue cases, January 2022

Summary

61 Note de synthèse: position de l'OMS à propos du vaccin antipaludique – mars 2022

76 Rapport mensuel des cas de dengue, janvier 2022

**Malaria vaccine: WHO position paper – March 2022**

**Introduction**

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and combinations of vaccines against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale immunization programmes. They summarize essential background information on diseases and vaccines and conclude with the current WHO position on the use of vaccines worldwide.

The papers have been reviewed by external experts and WHO staff and reviewed and endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization (<https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization>). This paper has also been reviewed and endorsed by the WHO Malaria Policy Advisory Group (MPAG) (<https://www.who.int/groups/malaria-policy-advisory-group>). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) method was used to assess systematically the quality of the available evidence. The MAGI and MPAG decision-making process is reflected in “evidence-to-recommendation” tables. The processes followed for the preparation of vaccine position papers are described at: [www.who.int/immunization/policy/papers/position\\_paper\\_process.pdf](http://www.who.int/immunization/policy/papers/position_paper_process.pdf). The WHO Global Malaria Programme follows the WHO guidelines development process described at: <https://www.who.int/publications/i/item/9789241548960>. The WHO guidelines for malaria are available at: <https://app.magicapp.org/#/guideline/5701>. The position papers are intended for use mainly by national public health officials and managers of immunization

**Note de synthèse: position de l'OMS à propos du vaccin antipaludique – mars 2022**

**Introduction**

Conformément à son mandat, qui prévoit qu'elle conseille les États Membres en matière de politique sanitaire, l'OMS publie une série de notes de synthèse régulièrement mises à jour sur les vaccins et les associations vaccinales contre les maladies ayant une incidence sur la santé publique internationale. Ces notes portent principalement sur l'utilisation des vaccins dans le cadre de programmes de vaccination à grande échelle. Elles résument les informations essentielles sur les maladies et les vaccins associés et présentent en conclusion la position actuelle de l'OMS concernant l'utilisation de ces vaccins dans le contexte mondial.

Ces notes ont été examinées par des experts externes et des membres du personnel de l'OMS, puis évaluées et approuvées par le Groupe stratégique consultatif d'experts (SAGE) de l'OMS sur la vaccination (<https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization>). Ce document a également été examiné et approuvé par le Groupe consultatif sur la politique de lutte contre le paludisme (MPAG) de l'OMS (<https://www.who.int/groups/malaria-policy-advisory-group>). La qualité des données disponibles a été évaluée de manière systématique au moyen de la méthode GRADE (Grading of Recommendations Assessment, Development and Evaluation). Le processus de décision de SAGE et du MPAG est reflété dans les tableaux des données à l'appui des recommandations. La procédure suivie pour élaborer les notes de synthèse sur les vaccins est décrite dans le document: [www.who.int/immunization/policy/papers/position\\_paper\\_process.pdf](http://www.who.int/immunization/policy/papers/position_paper_process.pdf). Le Programme mondial de lutte contre le paludisme de l'OMS suit le processus d'élaboration des lignes directrices de l'OMS décrit dans le manuel disponible à l'adresse: <https://www.who.int/publications/i/item/9789241548960>. Les lignes directrices de l'OMS sur le paludisme sont disponibles à l'adresse: <https://app.magicapp.org/#/guideline/5701>. Les notes de

# WHO Guidelines for malaria

March 2022

PDF version

<https://www.who.int/publications/i/item/guidelines-for-malaria>



WHO GUIDELINES

for malaria

31 March 2022



World Health Organization

# MAGICapp Online platform

<https://app.magicapp.org/#/guideline/5701>



WHO Guidelines for malaria - 31 March 2022

Menu

1 ABBREVIATIONS

ACT	artemisinin-based combination therapy
ANC	antenatal care
BCC	behaviour change communication
bw	body weight

More >

2 EXECUTIVE SUMMARY

The consolidated *WHO Guidelines for malaria* present all of the current WHO recommendations for malaria. These are the product of careful evaluation following standardized methods as part of the [WHO process for developing guidelines](#).

- evidence-based recommendations pertaining to vector control tools, te...

More >

3 INTRODUCTION

Background

Malaria continues to cause unacceptably high levels of disease

17



Health Topics ▾

Countries ▾

Newsroom ▾

Emergencies ▾

[Home](#) / [News](#) / WHO recommends groundbreaking malaria vaccine for children at risk

# WHO recommends groundbreaking malaria vaccine for children at risk

## Historic RTS,S/AS01 recommendation can reinvigorate the fight against malaria

6 October 2021 | News release | Geneva | Reading time: 3 min (859 words)

The World Health Organization (WHO) is recommending widespread use of the RTS,S/AS01 (RTS,S) malaria vaccine among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission. The recommendation is based on results from an ongoing pilot programme in Ghana, Kenya and Malawi that has reached more than 800 000 children since 2019.



*This long-awaited vaccine, developed in Africa, by African scientists, is a breakthrough for science, child health and malaria control... This vaccine is a gift to the world, but its value will be felt most in Africa, because that's where the burden of malaria is greatest.*

**WHO Director-General Dr Tedros Adhanom Ghebreyesus.**

## In summary: health research constitutes

- A global, regional and national **strategic need**
- Clinical trials constitute a cornerstone of medical research and are a critical component of the research and development process for new technologies, including drugs, medical devices, and treatment protocols.
- Clinical trials can have significant **economic implications** for countries. Hosting trials attracts investments from companies, which can lead to job creation, increased revenue, and the development of local expertise in research and development. A favorable environment for clinical trials can stimulate economic growth and create opportunities for technology implementation.

- **Regulatory Environment**: The regulatory framework and approval processes for clinical trials play a crucial role in determining the pace of technology implementation. Countries with efficient and transparent regulatory systems can attract more clinical trials, leading to earlier adoption and implementation of new technologies.
- **Competition** to attract clinical trials is increasing between countries and regions

Countries actively engaged in clinical trials tend to have a higher likelihood of early access to new technologies and improved healthcare outcomes.

Hosting clinical trials contributes to **capacity building**, collaboration, **policy development**, and patient engagement, all of which influence the implementation of new technologies in healthcare systems.