

Community Access to Rectal Artesunate for Malaria (CARAMAL)

Addressing the burden of malaria deaths by optimizing the use of rectal artesunate



What is severe malaria?

According to WHO (3rd edition malaria guidelines):

Severe falciparum malaria: one or more of the following, occurring in the absence of an identified alternative cause and in the presence of *P. falciparum* asexual parasitaemia

- Impaired consciousness
- Prostration
- Multiple convulsions
- Hypoglycaemia
- Severe malaria anaemia
- Renal impairment
- Jaundice
- Pulmonary oedema
- Significant bleeding
- Shock
- Acidosis
- Hyperparasitaemia >10%

iCCM: Integrated Community Case Management is an equity-focused strategy that complements and extends the reach of public health services by providing timely and effective treatment of malaria, pneumonia and diarrhoea to populations with limited access to facility-based health care providers, and especially to children under 5 (WHO)

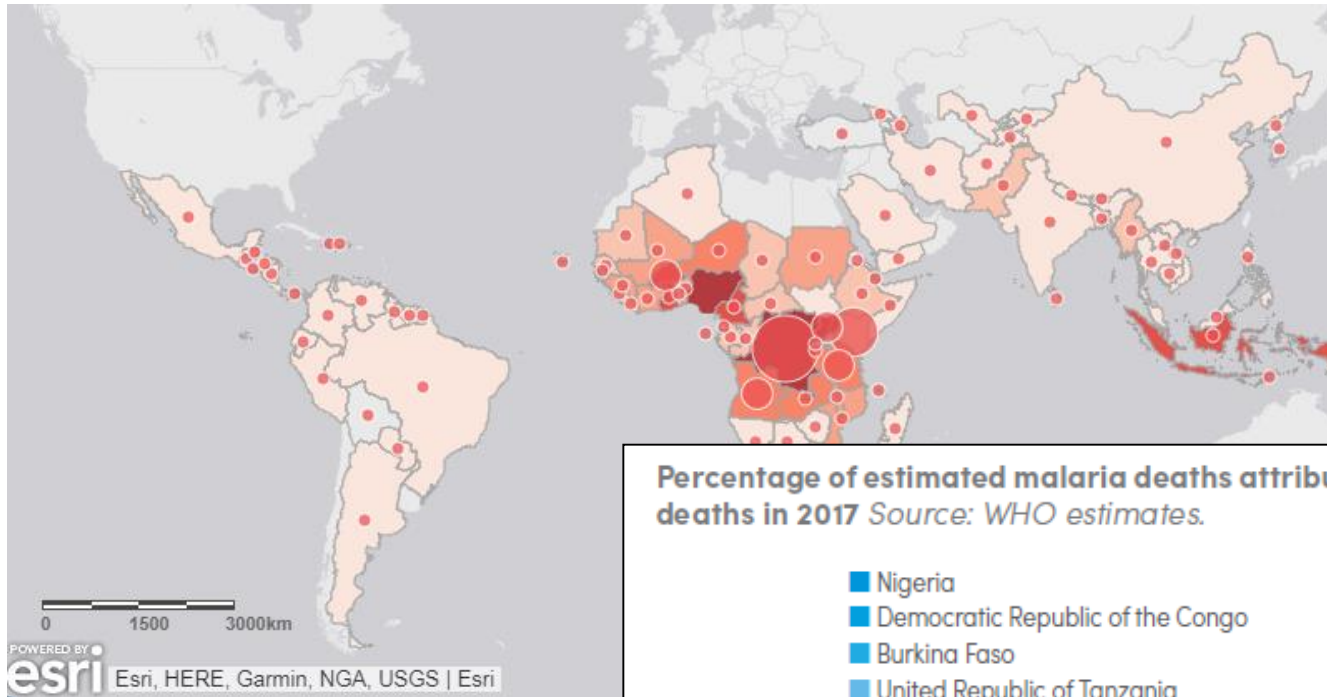
According to iCCM: Children with one or more danger sign: cough for 14 days or more, diarrhoea for 14 days or more, blood in stool, fever for last 7 days or more, convulsions, not able to drink or eat anything, vomits everything, has HIV and any other illness, or unusually sleepy or unconscious (Caring for Sick Child in the Community 2014)

According to National Guidelines (i.e., DRC): Severe malaria is defined at community level- as danger signs + fever



The burden of malaria

445,000 malaria deaths in 2016



Inpatient malaria cases and attr
Severe Malaria Observatory

- The majority of malaria inpatient deaths are in West, Central, and East Africa
- 80% in 15 countries
- DRC, Nigeria, Uganda: **173,000** deaths

Percentage of estimated malaria deaths attributable to the 18 countries with nearly 80% of global malaria deaths in 2017 Source: WHO estimates.



WHO: World Health Organization.

How do you treat severe malaria?

The WHO Guidelines for the Treatment of Malaria 3rd Edition strongly recommends injectable artesunate for treatment of severe malaria

Treating severe malaria

Treat adults and children with severe malaria (including infants, pregnant women in all trimesters and lactating women) with intravenous or intramuscular artesunate for at least 24 h and until they can tolerate oral medication. Once a patient has received at least 24 h of parenteral therapy and can tolerate oral therapy, complete treatment with 3 days of an ACT (add single dose primaquine in areas of low transmission).

Strong recommendation, high-quality evidence

Revised dose recommendation for parenteral artesunate in young children

Children weighing < 20 kg should receive a higher dose of artesunate (3 mg/kg bw per dose) than larger children and adults (2.4 mg/kg bw per dose) to ensure equivalent exposure to the drug.

Strong recommendation based on pharmacokinetic modelling

Parenteral alternatives when artesunate is not available

If parenteral artesunate is not available, use artemether in preference to quinine for treating children and adults with severe malaria.

Conditional recommendation, low-quality evidence

If Injectable artesunate is not readily available...

- Rectal artesunate (RAS) is recommended by WHO for pre-referral treatment of children under six with severe malaria danger signs
- RAS rapidly (within 24 hours) clears 90% or more of malaria parasites
- In children younger than six years of age who cannot reach a facility in less than six hours, RAS can reduce the risk of death or permanent disability by up to 50%



- RAS, however, is not complete treatment; linkages must exist between communities and facilities that facilitate smooth, timely completion of referral to a well-equipped and capable health system for treatment with injectable artesunate and a full course of ACTs

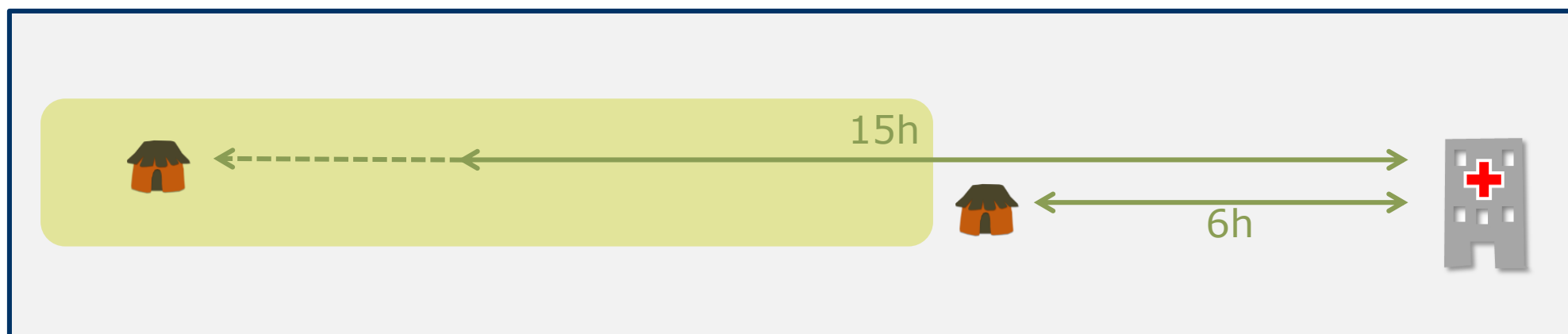
Scientific basis for implementation of pre-referral RAS

Pre-referral rectal artesunate to prevent death and disability in severe malaria: a placebo-controlled trial

M F Gomes, M A Faiz, J O Gyapong, M Warsame, T Agbenyega, A Babiker, F Baiden, E B Yunus, F Binka, C Clerk, P Folb, R Hassan, M A Hossain, O Kimbute, A Kitua, S Krishna, C Makasi, N Mensah, Z Mrango, P Olliaro, R Peto, T J Peto, M R Rahman, I Ribeiro, R Samad, N J White, for the Study 13 Research Group*

Lancet 2009


- In patients < 6 years of age not in clinic after more than 6 h, half were still not there after more than 15 h



In these patients, pre-referral rectal artesunate **significantly reduced death or permanent disability**

29/1566 [1·9%] vs 57/1519 [3·8%], **risk ratio 0·49** [95% CI 0·32–0·77]

What are the requirements for effective and complete severe malaria case management?



ASSESS AGE AND WEIGHT

Between 6 months to less than 6 years.

RECOGNIZE THE DANGER SIGNS

A febrile child or a child with recent history of fever with one or many danger signs:

- and/or → Unconscious or Lethargic
- and/or → Not able to drink or eat
- and/or → Vomits everything
- Seizing or Convulsing



TRANSFER URGENTLY

The child must be referred **immediately** to the nearest hospital or health care facility for a full course of antimalarial medicine by IV or IM.

1. Recognition of potential malaria infection and the need to seek care in a timely fashion by the child's caregiver

2. Recognition of the illness and its severity by the CHW or primary care provider

3. Appropriate administration of QA RAS

4. Referral to a sufficiently equipped, higher-level health facility able to manage the sick child with parenteral treatment

5. Completion of the referral by the caregiver

6. Proper severe malaria case management at the higher-level health facility



ADMINISTER RECTAL ARTESUNATE

The community health worker prepares the child and administers **rectal artesunate**.

Treating severe malaria

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Community Access to Rectal Artesunate for Malaria (CARAMAL) 2018-2020

- **CARAMAL** introduces rectal artesunate (RAS) at CHW level under real world settings
- CARAMAL will increase access to QA rectal artesunate (RAS) as part of strengthened severe malaria case management systems through increased demand and adoption, thereby reducing severe malaria case fatality rates in children.
- Project outputs
 - QA RAS made available
 - RAS introduced as pre-referral treatment
 - Evidence generated and shared on use of RAS
 - Transition to evidence-based and step-wise scale-up



Funding agency



Project coordination



iCCM implementation / RAS Implementation

Swiss TPH



Operational research







Country Research Partners



Supporting partners



CARAMAL Operational Research Objectives

				
Project area	DRC Kenge, Kingandu and Ipamu Health Zones	Nigeria Adamawa State, Fufore, Mayo-Belwa, Song LGAs	Uganda Apac, Kole and Oyam Districts	Total
Population	619,000	689,000	992,000	2,300,000
Pop. <5 years	112,000	212,000	176,000	500,000

Goal Contribute to **reducing malaria mortality in children** by improving the community management of suspected severe malaria.

Advance the **development of operational guidance** for the scale-up of pre-referral RAS for severe malaria

Research questions

- What are **minimal requirements** to ensure that RAS is an effective part of the continuum of care from the community to a referral facility?
- What are **unintended consequences** of scaled implementation at all levels of care, and how can they be addressed?
- Is there **use of RAS beyond the recommended guidelines**?
- Can the introduction of pre-referral RAS **reduce severe malaria case fatality ratio** over time under real-world operational circumstances?
- What are **costs and cost-effectiveness** of scaling up RAS?

Project status and preliminary observations

INFORMATION GATHERING & DATA GENERATION

- Referral health facility assessments conducted (Q3-Q4 2017)
- RAS landscaping assessment completed
- Patient Surveillance System (PSS) launched and in operation across all three countries
- Household Survey (HHS) and Health Care Provider Survey (HCPS) complete in all three countries
- Artemisinin resistance monitoring ongoing

	Gaps identified	Action taken
DRC	<p>1. Training: 56% of facilities with at least 1 MD trained on SM CM; 69% of facilities with at least 1 NO trained in SM CM</p> <p>2. Inj AS availability: 50% of facilities visited stocked out of Inj AS on day of visit; 81% of facilities experienced prolonged stock outs (some up to 90 days)</p>	<p>1. SM CM TOT (July 2018) for 16 provincial health management team members; training of 71 RHF providers in 3 target health zones (Kenge, Kingandu, Ipamu)</p> <p>2. Procurement of 1,000 viles of Inj AS to ensure availability of treatment post-referral</p>
Nigeria	<p>1. Training: 54% of facilities lacked personnel trained in SM CM; 38% of facilities with MD trained in SM CM; 15% of facilities with a NO trained in SM CM</p> <p>2. Inj AS availability: 69% of facilities equipped with Inj AS on day of visit; 36% of facilities reported Inj AS stock outs within last 12 mos</p>	<p>1. 3-day SM CM training (May 2018) for 35 health workers (doctors, pediatric care nurses, general care nurses) from 17 RHF in Adamawa</p> <p>2. Secured 44,000 doses of Inj AS (sourced from GF) for Adamawa. Staggered distribution between 2018 and 2019</p>
Uganda	<p>1. Training: 23% of facilities with MD trained in SM CM; 59% of facilities with NO trained in SM CM; many providers hadn't been trained in over 2 years</p> <p>2. Patient and referral tracking</p>	<p>1. SM CM training (June 2018) for 104 RHF health workers</p> <p>2. Patient identifier embedded in mTRAC to help build and track referral system</p>

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IMPLEMENTATION

- Secured WHO pre-qualification for 100mg RAS products from Cipla and Strides
- Supported RAS quantification exercises and placement of orders in three project countries
- Supportive interventions (mentoring, training) implemented at referral health facilities
- Development of RAS training materials for inclusion in iCCM curricula
- Over 7,000 CHWs trained in administration of RAS across all three countries

NON-PROJECT COUNTRY ENGAGEMENT

- 53% of African countries (30/56) have included RAS in their National Malaria Treatment Guidelines
- 56% (17/30) of those have recommendations aligned with the latest WHO treatment guidelines
- Light-touch support to non-project countries being pursued through key partners (e.g., PMI, MMV) and ministries directly

PRELIMINARY OBSERVATIONS

- Capacity of existing iCCM systems to expand to severe malaria CM
- Challenges with referral between community and health system
- Persistent use of quinine for treatment of severe malaria patients
- Treatment seeking in private sector

Questions/Comments?