

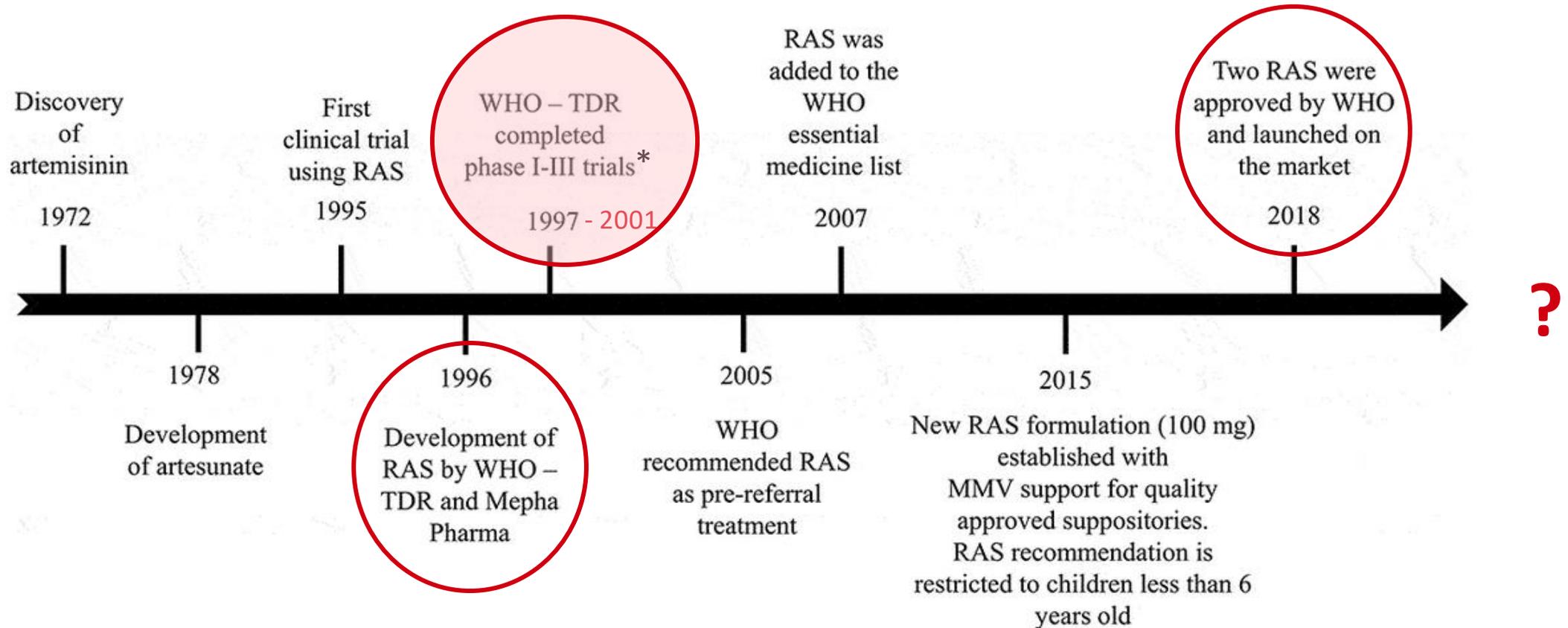


## **Understanding and improving case management of severe febrile illness in highly malaria-endemic settings: an observational implementation study in the Democratic Republic of the Congo, Nigeria and Uganda**

Aita Signorell, Manuel Hetzel, Antoinette Tshetu, Elizabeth Omoluabi, Phyllis Awor, Mark Lambiris, Nina Brunner, Giulia Delvento, Tristan Lee, Jean Okitawutshu, Jean-Claude Kalenga, Babatunde Akano, Kazeem Ayodeji, Charles Okon, Ocheche Yusuf, Prosciova Athieno, Joseph Kimera, Gloria Tumukunde, Irene Angiro, Valentina Buj, Theodoor Visser, Harriet Napier, Christian Lengeler, Christian Burri

# The valley of death: translation and take-up of evidence into real-world settings

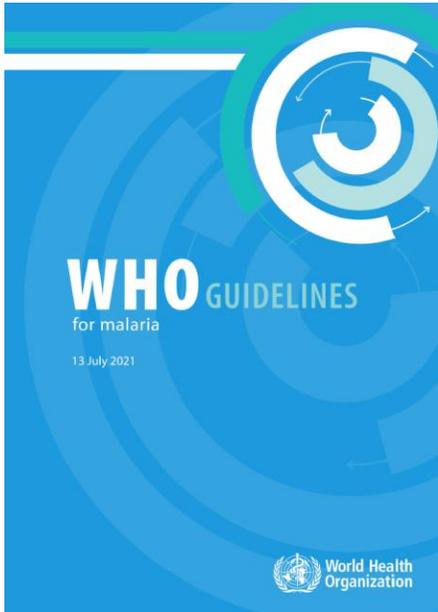
## Timeline of rectal artesunate (RAS) development:



Source: Laís Pessanha de Carvalho, Andrea Kreidenweiss & Jana Held (2021) The preclinical discovery and development of rectal artesunate for the treatment of malaria in young children: a review of the evidence, *Expert Opinion on Drug Discovery*, 16:1, 13-22, DOI: 10.1080/17460441.2020.1804357

\* Gomes MF, et al. *Lancet*. 2009

# Pre-referral rectal artesunate: current recommendations



Where intramuscular injections of artesunate are not available, treat children < 6 years with a single rectal dose (10 mg/kg bw) of artesunate, and refer immediately to an appropriate facility for further care. Do not use rectal artesunate in older children and adults.

Full treatment includes

1. parenteral artesunate for at least 24 hours, then
2. full course of artemisinin-based combination therapy (ACT)

1. What is the optimal way of rolling out RAS on a large (national) scale?
2. What is the effect of RAS implemented without major supportive interventions?

**Effectiveness vs. Efficacy**

# CARAMAL population coverage



DR Congo

Nigeria

Uganda

Total

PSS



**Project area**

Kenge, Kingandu and Ipamu Health Zones

Adamawa State, Fufore, Mayo-Belwa, Song LGAs

Apac, Kole and Oyam Districts

**Population**

785,967

746,949

995,986

**2,528,902**

**< 5 years**

268,197

130,430

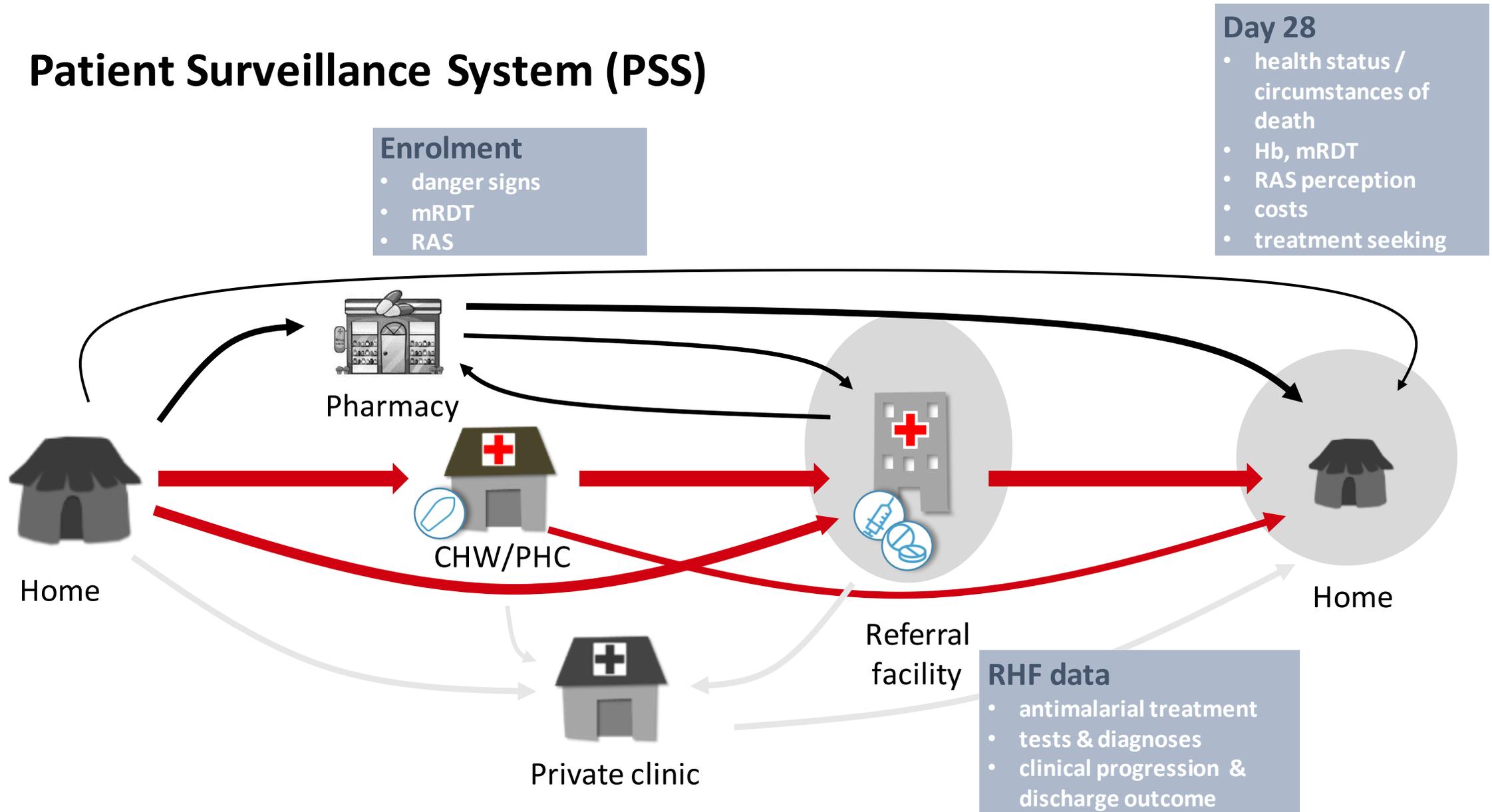
200,518

**476,054**

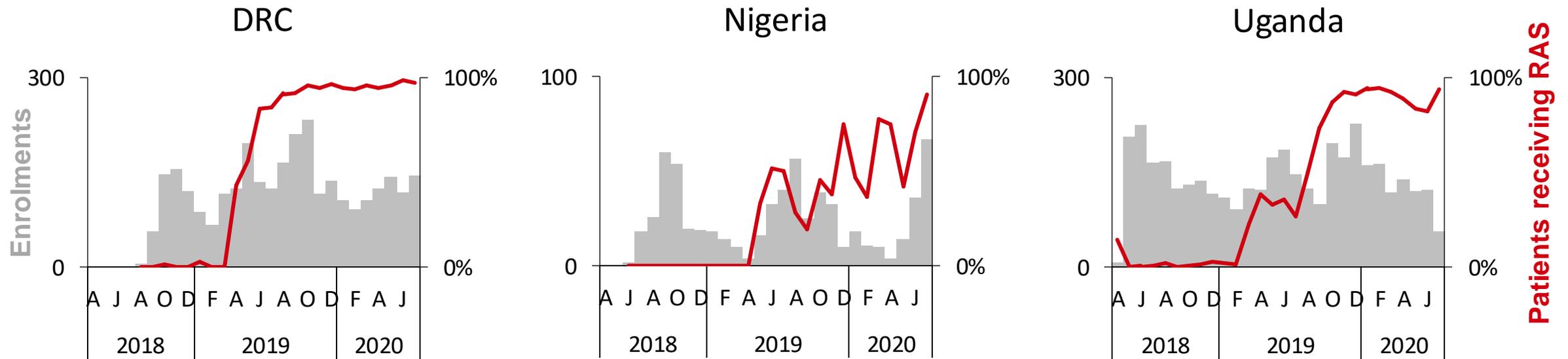
**13,758**

<https://www.worldpop.org> (2018)

# Patient Surveillance System (PSS)



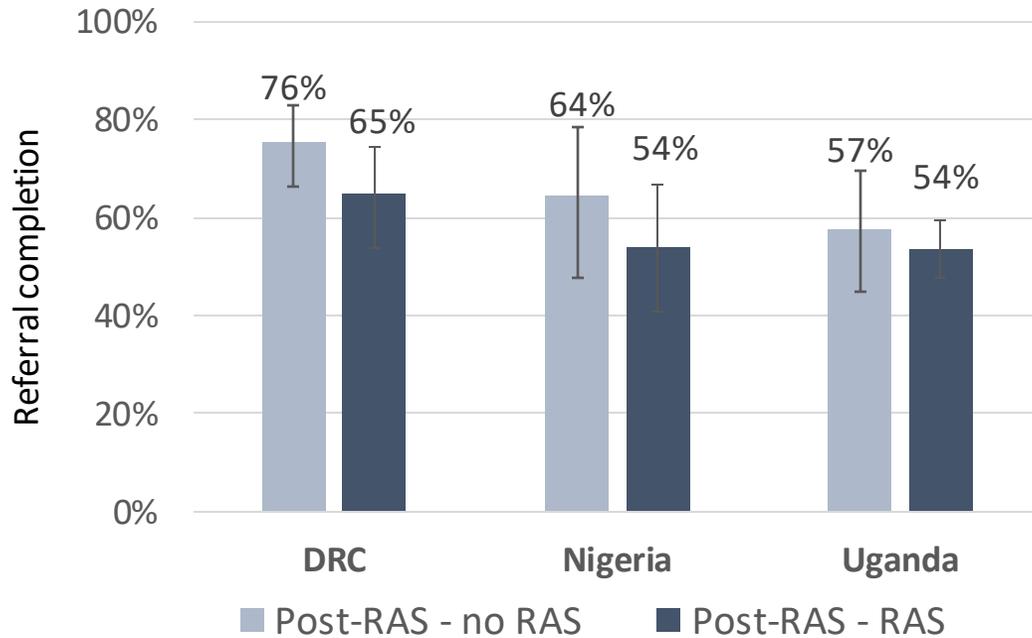
# RAS uptake



Mean percentage of patients receiving RAS in the post-roll-out phase

- DRC: 88%
- Nigeria: 52%
- Uganda: 70%

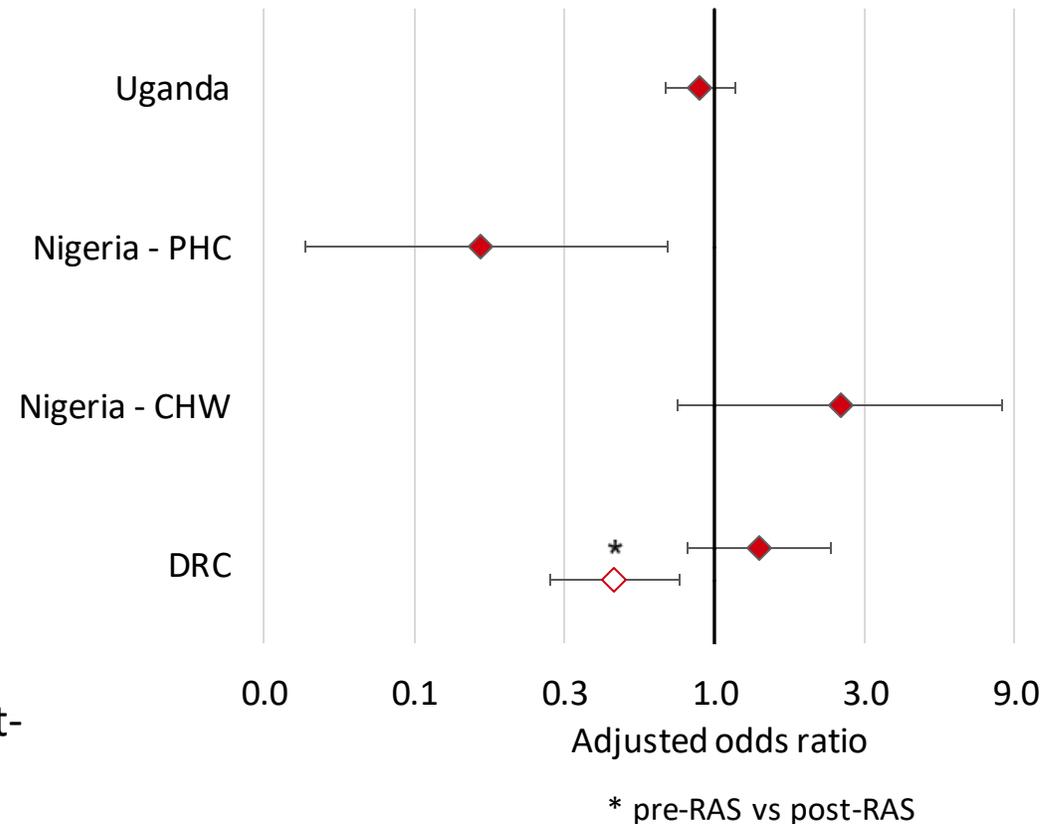
# Referral completion



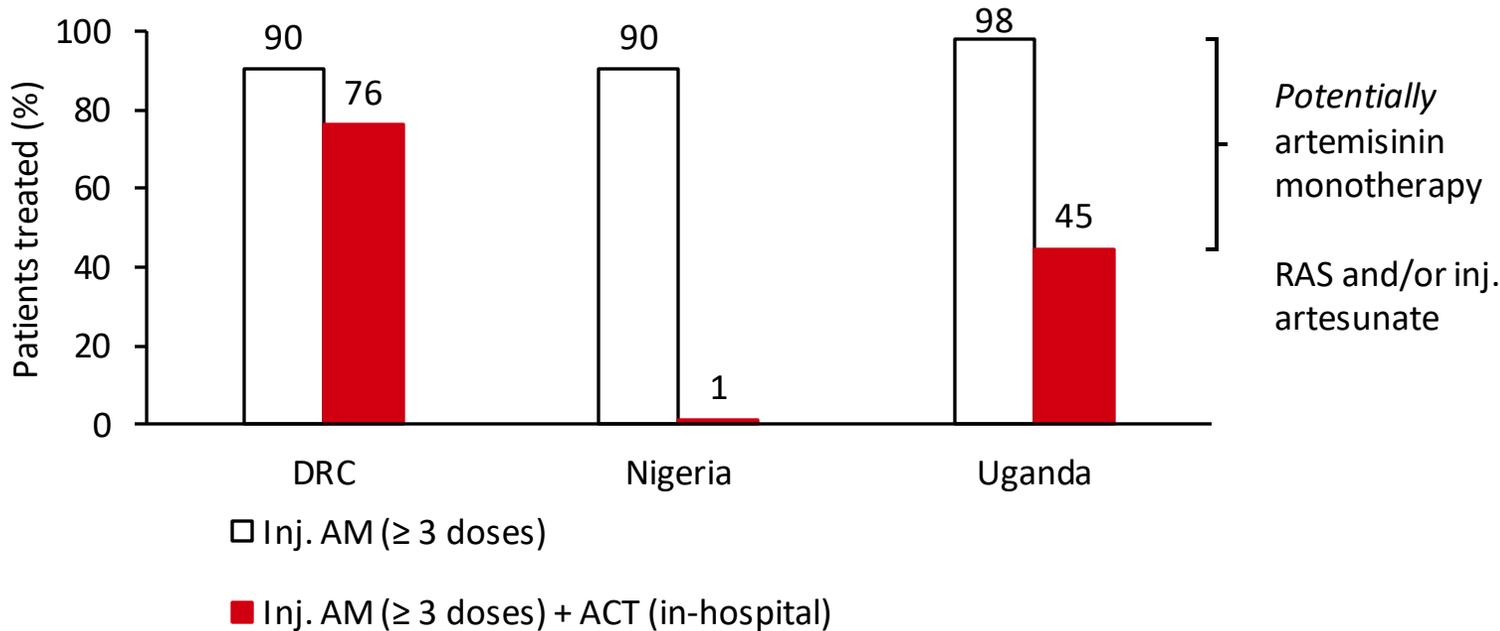
- In all countries, referral completion to a RHF was slightly lower among RAS users compared to RAS non-users (post-RAS phase)

➤ **Treatment of children who don't complete referral?**

## RAS use and referral completion Post-RAS period

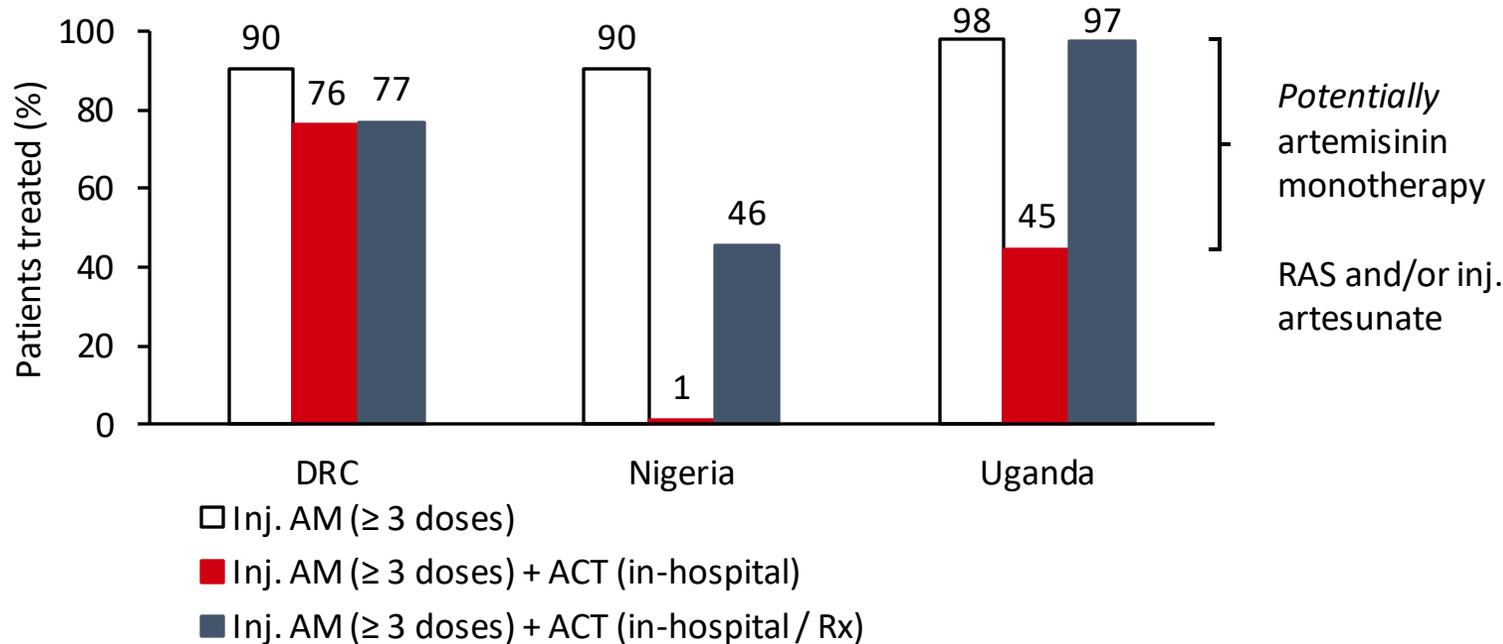


# Severe malaria treatment at referral facilities (post-RAS)



- Use of injectable antimalarials was high in all three countries
- A full course of severe malaria treatment (parenteral antimalarial + ACT) was high in DRC (76.2%), moderate in Uganda (44.7%) and very low in Nigeria (1.2%)

# Severe malaria treatment at referral facilities (post-RAS)



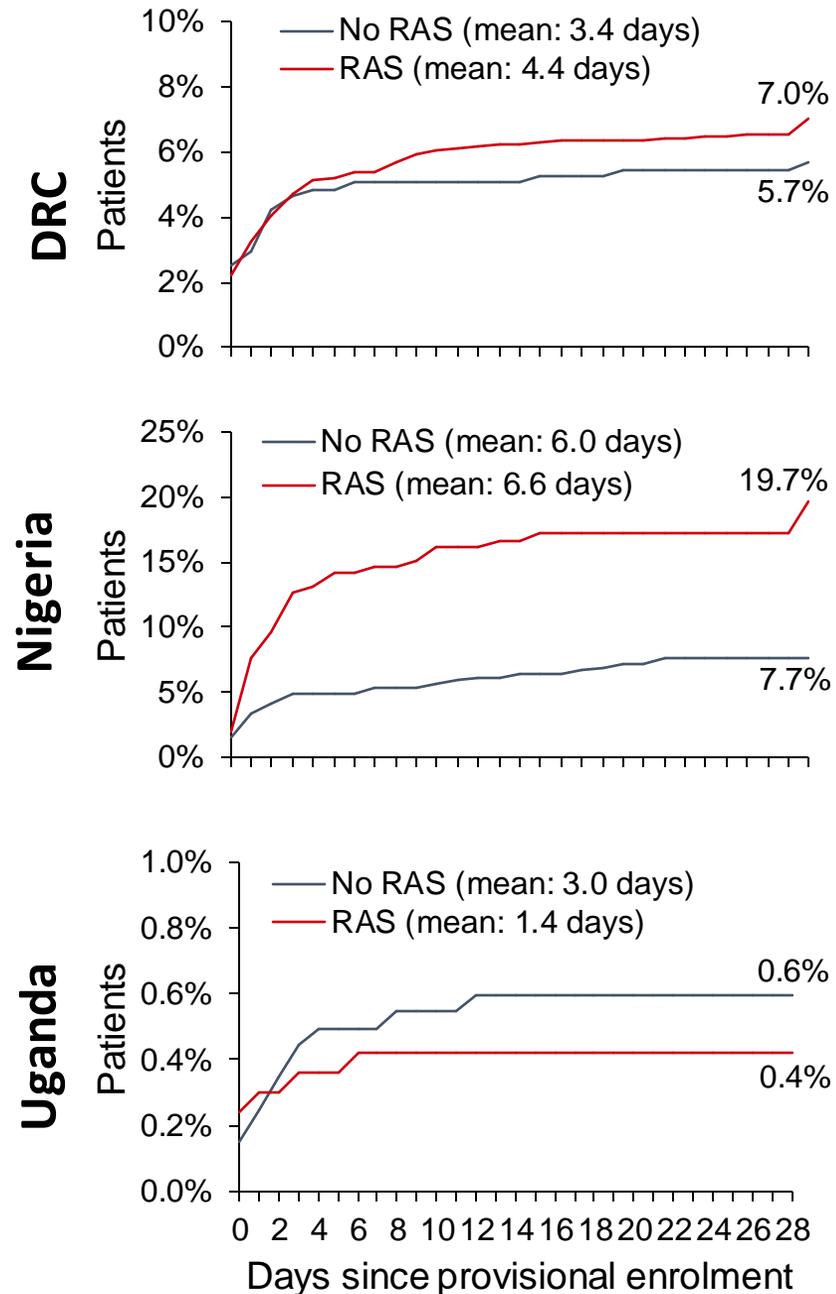
- Use of injectable antimalarials was high in all three countries
- A full course of severe malaria treatment (parenteral antimalarial + ACT) was high in DRC (76.2%), moderate in Uganda (44.7%) and very low in Nigeria (1.2%)
- In Uganda and Nigeria, caretakers were mostly given a prescription instead of the treatment

Not competing treatment with an ACT leads to

- **incomplete parasite clearance**
- **monotherapy, and as a consequence, a higher risk of developing artemisinin resistance**

# Case Fatality Rates (D28)

- The CFR was 6.7% (135/2011) in DRC, 11.7% (69/589) in Nigeria, and only 0.5% (19/3686) in Uganda ( $p < 0.001$ )
- Mortality was higher in the RAS group, marginally so in DRC and Uganda, but very much so in Nigeria
- Usually death occurred within a few days of enrolment
- Most deaths occurred in a health facility (DRC 73%, Nigeria 49%, Uganda 42%)



# Discussion

- In the CARAMAL countries, RAS was introduced in areas with weak health systems and impoverished communities; multiple severe system deficiencies were observed - leading to low cure rates and high case fatality rates.
- RAS is part of the continuum of care for severe malaria – without considering the health system as a whole, including treatment seeking patterns, supplies of multiple commodities, referrals, post-referral treatment and supervision, reducing case fatality from severe malaria and other major childhood diseases is unlikely to be achieved.
- Under current health system conditions, it is unlikely that RAS offers a care and child survival benefit; it could even be harmful by reducing referrals and selecting for drug resistance.

# CARAMAL Consortium



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