

# Promising antimalarial drug proves ineffective at saving children's lives

December 20 2022

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Credit: Matthis Kleeb/Swiss TPH

Rectal artesunate (RAS), a promising antimalarial drug, proves ineffective at saving the lives of young children suffering from severe malaria, according to the results of a new study conducted by the Swiss

Tropical and Public Health Institute (Swiss TPH) and partners. A viewpoint about these findings was published today in *The Lancet Infectious Diseases*.

The study, which investigated a large-scale roll-out of RAS in the DR Congo, Nigeria and Uganda, found that when used as an emergency treatment under [real-world conditions](#), RAS did not improve the odds of survival for [young children](#) with severe malaria.

"Our findings point to a very inconvenient but important issue," said Manuel Hetzel, Professor of Epidemiology at Swiss TPH and first author of the publication. "We found that the overall management of severe malaria cases is so poor, that adding a single product does not seem to make a positive difference. Our focus must be on investment in improving existing [health systems](#) instead of relying on individual interventions."

The [observational study](#), which included 6,200 severely ill children under the age of 5 years, found that in some instances, the children who received RAS were more likely to die than those who did not. "RAS was previously shown to have a beneficial effect if it is followed by adequate post-referral care at a hospital, which raised hopes in the malaria community," added Hetzel.

"But more often than not, children do not finish the entire treatment due to lack of transportation to hospitals, cost of transport and treatment, or poor quality of care at hospitals."

Pre-referral treatment with RAS is the administration of a single suppository by a community health worker or in a remote health facility as an [emergency treatment](#), in order to bridge the time until a child is admitted to a hospital where comprehensive post-referral care is available. Post-referral care for [severe malaria](#) includes treatment with

an injectable antimalarial, followed by a full oral course of artemisinin-based combination therapy (ACT), plus antibiotics and measures to manage potential complications.

## **Current recommendation by the WHO**

The current WHO guidance on using RAS as pre-referral treatment is based on a randomized controlled trial that took place between 2000 and 2006 in Ghana, Tanzania and Bangladesh. The trial offered limited guidance on introducing RAS at scale. "Under real-life conditions, many factors influence whether an individual is appropriately treated and cured, which is why interventions that work well in a controlled trial may not always fulfill their potential in real life," said Phyllis Awor, co-investigator of the study at the Makerere University School of Public Health in Uganda.

Based on the results of this new study, the WHO issued an Information Note in October 2021 recommending that countries either delay scale-up until further guidance on the safe implementation of RAS is made available, or urgently review the conditions under which it is currently being used. At present, the current WHO guidelines on RAS are under review by a team of WHO-appointed experts.

"The real-world evidence generated in our study should be taken into consideration before pushing for a large-scale roll-out of pre-referral RAS in systems that do not have a functioning continuum of care," said Hetzel. "Without a comprehensive approach that acknowledges the complex realities faced by caregivers and [health workers](#) in remote, underserved areas, children will continue to die from [malaria](#), and promising interventions such as RAS will fail to meet their full potential."

The Community Access to Rectal Artesunate for Malaria (CARAMAL)

project was an observational study that accompanied the introduction of pre-referral RAS in the Democratic Republic of the Congo (DRC), Nigeria and Uganda between 2018 and 2021. It is the first study of its kind to look at the introduction of quality-assured RAS in existing community-level health care systems at a large scale.

**More information:** Manuel W Hetzel et al, Pre-referral rectal artesunate: no cure for unhealthy systems, *The Lancet Infectious Diseases* (2022). [DOI: 10.1016/S1473-3099\(22\)00762-9](https://doi.org/10.1016/S1473-3099(22)00762-9)

Provided by Swiss Tropical and Public Health Institute

Citation: Promising antimalarial drug proves ineffective at saving children's lives (2022, December 20) retrieved 17 February 2023 from <https://medicalxpress.com/news/2022-12-antimalarial-drug-ineffective-children.html>

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