



Effects of restricting the use of Artesunate plus amodiaquine combination therapy to malaria cases confirmed by a dipstick test: A cluster randomised control trial

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Background

- Presumptive treatment for malaria (IMCI)
 - Justified on the basis of

PREVIOUS JUSTIFICATION	CHANGING TIMES
High malaria transmission	Reducing levels of transmission
Difficulty and or delay in laboratory confirmation	Improved Rapid Diagnostic kits HRP-2
Cheap anti-malarial	ACT 10 times and more expensive

- Over-diagnosis → Risk of false-negative diagnosis of other febrile illnesses
- Reducing transmission → accurate diagnosis
- RDTs has the potential to improve quality of diagnosis & treatment
- The accuracy of RDTs varies (epidemiological & programmatic)
 - Consequences of false negative diagnosis of malaria ?
 - Consequences of false positive diagnosis of another infection as malaria ?
- IPT → reduce malaria and anaemia
- Restricting ACT based on RDT means missed opportunity for IPT
- Effects of RDT based ACT on health outcomes particularly anaemia?

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Study outline

Stage 1: (March – November 2009)

Component A

Accuracy of RDT and the outcomes of treatment based on RDT results

Component B

Delivery system determinants of effective use of RDT based ACT

Stage 2: (January 2010 – December 2012)

Component A

Effects of restricted use of ACTs based on RDT results: a randomised controlled trial

Component B

Cost effectiveness analysis

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Stage 1, component A

Accuracy of RDT and the outcomes of treatment based on RDT results

Objectives:

- **Primary**
 - What is the sensitivity and specificity of RDT in Ghana to diagnose malaria?
- **Secondary**
 - What is the sensitivity and specificity of RDT to diagnose low parasite density malaria?
 - What is the sensitivity and specificity of microscopy to diagnose malaria?
 - What are common infectious agents in RDT+ and RDT- patients?
 - What is the prognosis of participants who had a false +ve or –ve diagnosis of malaria?

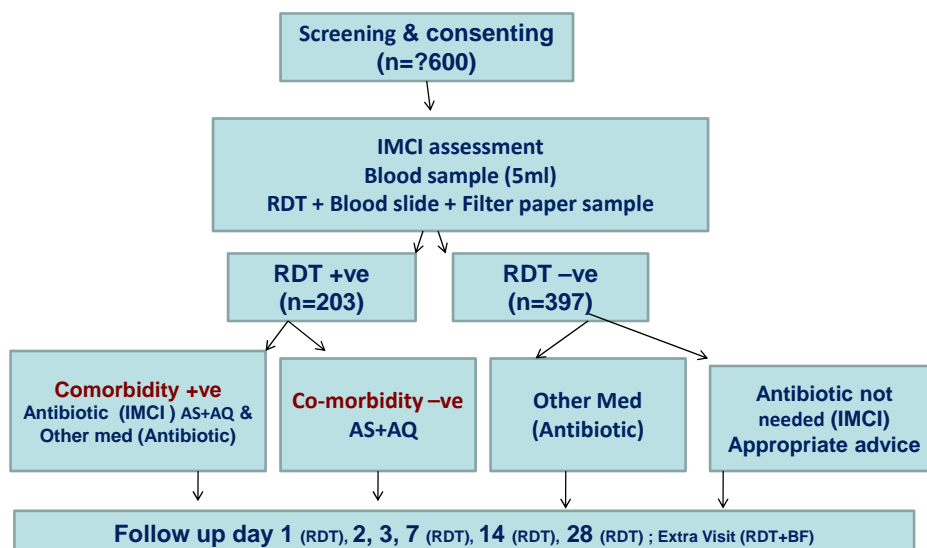
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Study site and population

- **Cohort study at the Kintampo District Hospital (KDH):** Prospectively recruited at the OPD
- **Inclusion criteria**
 - Suspected cases of uncomplicated malaria
 - Aged 3mths - 5yrs old
 - Willing to take part in the study;
 - Reside within 15 km radius of KDH
- **Exclusion criteria**
 - Severe malaria
 - Severe anaemia (Hb<8g/dl);
 - Severe malnutrition

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Stage 1 Component A: Study Design



Outcomes to be delivered by Q1 2010

- Accuracy of the RDT –Sensitivity
- Treatment outcome of clinical decision based on RDT results: Up to 28 days
- Usefulness of RDT in the follow-up of febrile cases
- Etiology of febrile illnesses (malaria, bacterial & viral)

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Stage 1 Component B

Delivery system determinants of effective use of RDT based ACT:

Research Question:

By how much would the health delivery system impact on the expected effect of RDT use?

Objectives:

Quantify the impact of decisions at each step in the process of delivering IMCI based correct treatment

Quantify the impact of decisions at each step in the process of delivering ACT based treatment for children in health facilities where RDT is in use

Model the provider and user determinants of diagnosis and treatment

Describe the factors that influence decisions at each step in the process of delivering IMCI based treatment

Model the determinants of treatment of those RDT negative for malaria parasite

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Methods

- Structured observations (5 hospitals and 10 health centres)
- Exit interviews with carers of febrile children under 5 years
- Semi-structured interviews with providers
- Outcome determination 7-14 days after clinic visit

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Stage B, Component A: Effects of restricted use of ACTs based on RDT results: a randomised controlled trial

- *Primary:*
 - Incidence of malaria in children 48 months of age?
- *Secondary:*
 - Incidence of severe anaemia?
 - Incidence of other severe febrile diseases?
 - Use of antibiotics for treating febrile illness?
 - Community perception of the quality of care and the treatment seeking behaviour
- **Cluster randomised two arm trial**
 - Health Centres as unit of randomisation

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STUDY DESIGN: HEALTH CENTER LEVEL CLUSTER-RANDOMISED TRIAL

- **Intervention** : RDT+ACT group (ACT offered to RDT positive cases only)
- **Control**: Clinical judgement +ACT group (ACT offered to all suspected cases of malaria by clinical judgement).

PHASE	Cohort enumeration (Baseline)	INTERVENTION
Duration	3-5months	24months
Goal	100 children aged 3mths – 24mths living within 10km radius of health center •Photo ID •Socio-demographics •Contextual factors	Randomized intervention Passive & Active (3mthly home-visits) surveillance •Fever •Morbidity questionnaire •Blood sample (slide , PCR + HB)
Cost-effectiveness		Cost of treatment of febrile children (RDT + ACT) Cost of treatment of febrile children (Clinical judgement + ACT) Mean number of sick days in children under 48 months of age

Outcome measures

- Incidence of severe anaemia
- Incidence of malaria
- Incidence of severe febrile illness
- Mean number of sick days
- Use of antibiotics

Stage 2, component B - Cost-effectiveness

(Data collection will run alongside Stage 2, component B)

- **Primary**
 - Cost effectiveness of RDT based ACT for treatment of children under 4 years compared with ACT based on clinical judgement?

- **Secondary**
 - Costs of alternative treatments where ACT is based on RDT results compared to ACT based on clinical judgement?

 - Cost implications for a District Health Management Team (DHMT) of making RDT based ACT policy?

 - Implications of the health insurance scheme for the cost effectiveness and equity of RDT based ACT?

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Summary

Two-Stage study evaluating

- ACCURACY & UTILITY OF RDT
- DETERMINANTS OF OPTIMAL ACT USE
- IMPACT ON TREATMENT OUTCOME

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ACKNOWLEDGEMENT

- Communities members and local authorities in the Brong Ahafo Region of Ghana
- National Malaria Control Program – Head & Staff
- Oversight & reviewers
 - KHRC Institutional Review Board
 - Ghana Health Service
 - LSHTM Ethical Review Committee
 - Data Safety Monitoring Committee
- Secretariat of the ACT Consortium

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Thank you



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