Some basic facts on combination therapy

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What are the problems with malaria?

- The disease
- The drugs
- The policies
- The finance
What are the problems with malaria (1)?

The disease

- Kills mainly children
- Pregnant women also at risk
- Majority of patients are poor
- Parasite has (can develop) ways of avoiding action of drugs
What are the problems with malaria (2)?

The drugs

- Availability
- Accessibility (physical/financial)
- Effectiveness (development of resistance to monotherapies)
Ways of addressing problem of resistance

- Discover new antimalarial drugs [slow, expensive]
- Rational use of what is available [= concept of combination therapy]
What is combination therapy (CT)?
COMBINATION THERAPY: DEFINITION

CT is the simultaneous use of two or more blood schizonticidal drugs with independent modes of action and different biochemical targets in the parasites.

CTs can be either fixed ratio combinations or multiple-drug therapy, in which components are co-administered in separate tablets or capsules.
What is the ideal combination?

- Two or more drugs with different modes of action. One should kill gametocytes. No resistance to either component.
- Rapid (within 24 h) achievement of $\text{EC}_{99}$
- Maintain MEC for 3-4 parasite life cycles
What is the ideal combination?

- Orally effective. Good oral bioavailability
- Duration of treatment \( \geq 3 \) days
- Simple dosing regimen
- Co-formulated; paediatric formulation
- Both components stable (reasonable shelf-life)
What is the ideal combination?

- Safe for use in all age groups
- No drug-drug interactions; (undesirable) drug-food interaction
- Affordable
- Effective against multi-drug resistant parasites (real life: adherence, quality, use, efficacy)
Are combination antimalarial drugs necessary?
Only if other factors are considered

1. Rational selection
2. Affordable prices
3. Sustainable financing
4. Reliable health and supply systems
Thank you