Selecting appropriate antimalarial drugs: a model for policy makers

Abbreviations of drug names used in this paper

AS – Artesunate (a derivative of artemisinin)

AQ – Amodiaquine

CDA – Chlorproguanil-dapsone-artesunate

SP – Sulphadoxine-pyrimethamine

Malaria deaths are increasing globally, mainly because the parasites that cause malaria are becoming resistant to the most commonly used drugs.

A new model based on data from the field can help to predict the effective lifespan of a drug before widespread resistance develops. The model focuses on drug combinations and can be applied to both current and potential treatments. It can be used to forecast the lifespan of a drug before parasites develop resistance in a range of combination treatments. This can be a valuable tool for policy makers and National Malaria Control programmes facing dilemmas in choosing appropriate treatment regimes of drugs known as antifolates.

Drug selection model

Previously it had been common practice to use combination therapy only when failure of the usual drug was imminent. The World Health Organization (WHO) now requires that a new antimalarial drug should always be used in combination with another antimalarial drug, not alone. The new model demonstrates startling evidence that if one drug is already failing to treat malaria, combination therapy that includes that drug will not work. The model can be used to judge whether any new single or combination treatment will be effective for long enough to make the cost and disruption of change in policy worthwhile.

The model is designed to be used by non-specialists and can be found on the Liverpool School of Tropical Medicine website at:

http://pcwww.liv.ac.uk/hastings/CTmodel.xls

The model can be adapted to the user's local conditions. The user must enter data on the mean number of drug treatments per patient each year and the proportion of malaria infections that will be treated with the drugs in question. This will produce results that can guide decision-making on the use of antimalarial drugs.

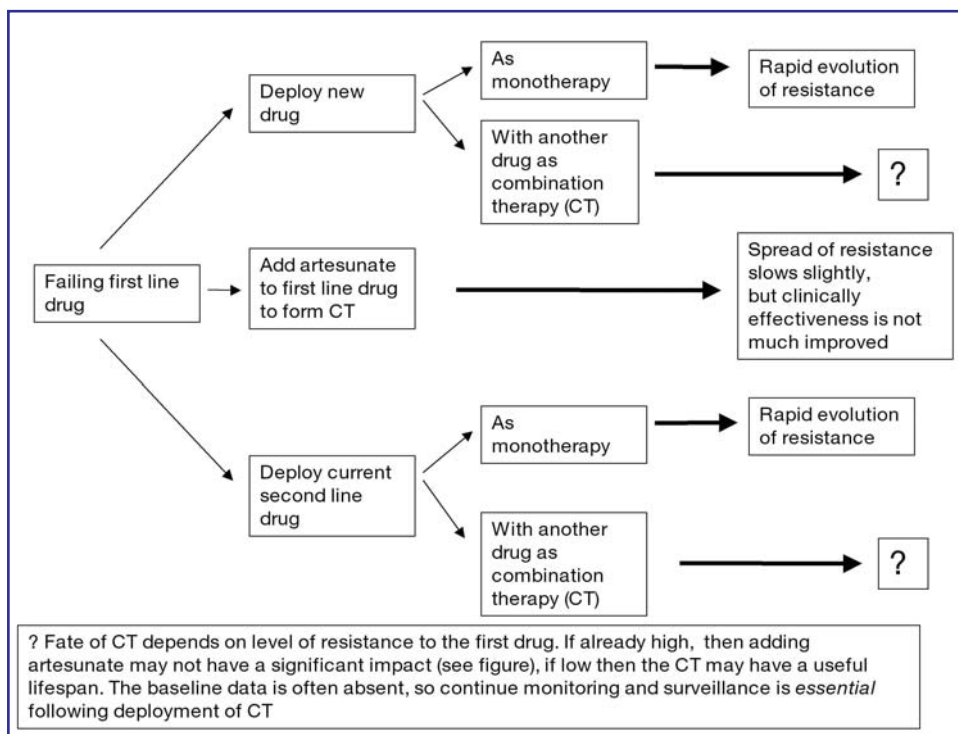Below and overleaf we present key recommendations from the model.

Key recommendations from the model

- It is critical to introduce combination therapy before parasites become resistant to either drug. Combination therapy is only effective if both drugs are still successful in treating the majority of malaria cases. Adding another drug to one that is already failing does not work.

- **Baseline data of resistance to malaria drugs is often absent, so continuous monitoring and surveillance are essential when combination therapy is introduced.**

- Combination therapies can be expensive, especially when using the drug AS. Where AS is unaffordable, combinations of less expensive drugs should be considered. However, this will be effective only if resistance has not developed to either drug in the combination.

- **Resistance to SP is common in Africa. Quick action is needed to determine whether there are any areas left where resistance to SP is low enough to allow it to be used in a combination therapy. West Africa is one place where this might still be possible.**

National Malaria Control Programme drug-specific recommendations

- National programmes that are considering a policy change from chloroquine to SP/AS or SP/AQ combination treatment should carefully assess the prevalence of resistance to SP. If resistance to SP is at a critical level, combining it with AS or AQ will not work.

- **National programmes that are considering introducing LapDap™ should use the model described in this paper to decide whether they should adopt LapDap™ immediately or wait for deployment of LapDap in combination with AS (CDA), which may be effective for longer.**

- If the cost of Artesunate combination treatment is too high, SP can be combined with AQ only in areas where resistance to either SP or AQ has not reached critical levels. This could be a crucial factor in controlling the effectiveness of newer treatments in the future.

- **In West Africa there is better potential for AQ/AS combination because a high level of resistance to AQ does not yet seem to have been reached.**

Below: Illustration of how to make an appropriate selection of drugs

? Fate of CT depends on level of resistance to the first drug. If already high, then adding artesunate may not have a significant impact (see figure), if low then the CT may have a useful lifespan. The baseline data is often absent, so continue monitoring and surveillance is *essential* following deployment of CT

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Reference

Watkins W., Sibley C. H., Hastings I. M. (2005) 'The search for effective and sustainable treatments for Plasmodium Falciparum malaria in Africa: A model of the selection of resistance by antifolate drugs and their combinations' in *American Journal of Tropical Medicine and Hygiene*, 72 (2), 2005, pp.163-173